**Eur**opean **Rev**iew for **Med**ical and **Pharmacol**ogical **Sci**ences 2011; 15: 601-636

# *Pharmacological drugs inducing ototoxicity, vestibular symptoms and tinnitus: a reasoned and updated guide*

G. CIANFRONE[1], D. PENTANGELO[1], F. CIANFRONE[2], F. MAZZEI[1], R. TURCHETTA[1], M.P. ORLANDO[1], G. ALTISSIMI[1]

[1]Department of Otolaryngology, Audiology and Phoniatrics, "Umberto I" University Hospital, Sapienza University, Rome (Italy);
[2]Institute of Otorhinolaryngology, School of Medicine, Catholic University of the Sacred Heart, Rome (Italy)

**Abstract. – The present work on drug-induced ototoxicity, tinnitus and vertigo represents the update and revision of a previous guide to adverse drug reactions for italian physicians (2005). The panorama of drug-induced side effects causing ototoxicity or symptoms such as tinnitus or dizziness and vertigo has enlarged in recent years, thanks to a better knowledge and a more specific attention of pharmaceutical firms and drug-control institutions. In daily clinical practice, there is a need for the family physician and the ENT specialist or audiologist (also in consideration of the possible medico-legal implications) to focus the attention on the possible risk of otological side effects. This would allow a clinical risk-benefit evaluation, weighing the possible clinical advantage in their field of competence against possible otological side-effects. The list of active ingredients and drugs is subdivided in categories based on their audiological and otoneurological side-effects, that have been signaled by the drug companies and/or ministerial notes. Drugs have also been subcategorized with regards to the field in which they are applied, the therapeutic indications and the clinical behaviour. They have also been organized in alphabetical order, for an easier consultation.**

**The guide above, even if initially conceived for being used in Italy, also presents a more general and international interest, expecially as for as the concepts of pharmacology and the features of the active ingredients are concerned.**

**The guide is, therefore, useful as for as we are concerned to any physician, regardless of the country he/she operates in.**

*Key Words:*

Pharmacovigilance, Side-effects, Ototoxicity, Tinnitus, Vertigo.

## *Introduction*

The panorama of the pharmacological origin iatrogenic noxae able to induce either harmful ototoxic effects or just a symptomatology like tinnitus or balance disturbances, without any harmful consequence, has widened in the last few years. The reason for this is the progress of scientific knowledge, the increased awareness of the pharmaceutical companies and of the institutions, which supervise pharmaceutical production.

Only through continuous updating and experience sharing it's possible to offer patients the certainty of receiving the treatment that is appropriate, safe and effective and based upon the most credited clinical studies. This approach is definitely challenging but necessary in order to attain positive effects towards the improvement of patient's conditions and quality of life.

In every day medical practice physicians, otolaryngologists and audiologists, need to focus on the risks of otologic side effects, also from a legal point of view. It will then be beneficial to have a wider variety of drugs of the same family at hand, therefore, having a wider range of options meeting the main therapeutic line. Physicians have to daily balance the drug between effectiveness and safety; in any case the optimization of the pharmacological/therapeutic ratio has to be strictly related to the compromise between clinical advantages and undesired side effects.

Today's work on ototoxic, tinnitus and vertigo induced drugs is a revision and an update of what was previously published in 2005, regarding undesired side effects of drugs of the otoaudiologic field, which has had a positive result and has drawn interest from both general and specialized practitioners[1].

*Corresponding Author:* Giancarlo Cianfrone, MD; e-mail: giancarlo.cianfrone@uniroma1.it

In the specialised medical practice of otolaryngology and audiology there is the need to evaluate the patient from a pharmaceutical point of view to assess the potential risks of otologic side effects. This will allow the evaluation of clinical advantages versus otologic adverse events. The aim is to optimise the drug administration schedule in order to obtain a therapeutic improvement while sustaining the least number of side effects in the otovestibular apparatus. Sometimes symptomatic or harmful effects do not show up immediately after the first treatment but after a certain time, varying from subject to subject. This delay could be explained by an increase in the organs vulnerability and/or a minimal asymptomatic event after the first treatment and will later be revealed by the next dosage. In other instances side effects could be induced by following non-pathogenic non-iatrogenic noxae (trauma, noise, infections, circulatory, metabolic or endocrynologic disorders) or iatrogenic (oto-surgery).

### Pharmacological Action Influencing Factors

Factors affecting the pharmacological action are: the drug itself (dosage, chemical, physical or physical/chemical properties), the combination with other drugs or substances (interaction and other types of interference), pharmaceutical preparation (which affects the bio-availability of the active principle) or other factors relating to the patient using the drug and by the space/time context in which the drug is administered.

It is well known how the season, the climate, the altitude, the temperature etc. may interfere with the pharmacological action determining sometimes a change from being curative to being toxic. Ultimately the patient is the factor that most affects the pharmacological action, it depends on the general physiological state of the subject, on the pathological conditions involved, on his capability to metabolise and so eliminate the drug, on his sensitivity, which could be high (up to the induction of hyper-sensitivity phenomena both idiosyncratic or allergic) or low. At last factors like gender, age, race, body weight and even social condition and psychological profile are also important in determining or influencing the pharmacological action[2].

### Interactions

An additional consideration has to be given to pharmaco-dynamic and pharmaco-kinetic actions between different drugs used simultaneously. The current, sometimes marginal, knowledge of drug behaviours make interactions a delicate issue.

The effects of a drug could be affected by the presence of either of another drug or of food generating an interaction that could be dangerous when causing an increase in toxicity or a decrease in effectiveness. Food creates rare and less important clinical interactions by effecting the speed and the degree of absorption of a drug. Fortunately combinations of drugs to be avoided are only a handful and many drugs with interaction issues can be administered simultaneously by taking proper precautions.

Pharmaco-dynamic interactions take place when the effects of a drug are interfered with by the presence of another drug on the action site. They arise between drugs which share the same or opposite therapeutic effects and that act upon the same physiologic system i.e. sedatives that affect brain and respiratory functions. On the contrary, certain drugs could reduce the effectiveness of others because they compete for the same receptors.

Pharmaco-kinetic interactions can take place at the following levels:

**Absorption:** affecting bioavailability of a drug by altering the absorption coefficient or the total quantity of the drug absorbed;

**Distribution:** the circulation of a drug can be in an inactive form, binded to proteins, or in an active form, not binded; administration of drugs competing for the same proteic linkage might cause an increase in the "free quota" of the drug and consequently its activity;

**Metabolism:** interactions can take place between drugs metabolized by the same enzymatic system, they can act as enzymatic inductors accelerating the metabolism of the other drug and so reducing its effectiveness, or as enzymatic inhibitors slowing down the metabolism of the other drug creating accumulation and thus an increased risk for dosage related side effects;

**Elimination of the drug:** interactions can cause an alteration of both active tubular separation and glomerular filtration during renal clearance of certain drugs.

We can understand that the problem of drug interactions during co-administration is important and delicate. As an example, on "Medicines for Children", the paediatric therapeutic formulary issued by the Royal College of Paediatricians

and Child Health, which is also included in the "Children Drugs User Guide" published by the Italian Department of Health[3], the combination of an aminoglycoside like amikacin with vancocymin, ciclosporin, cisplatin, furosemide or amphotericin might increase the risk for ototoxicity and nephrotoxicity, but even the association of amikacin with non-ototoxic drugs like cephalosporin, according to the source, might increase the risk for ototoxicity.

To this day it is not possible to anticipate the otologic effects of a single drug, of a combination of drugs, or of drugs combined with non-iatrogenic events such as exposition to noise. It looks like predisposition or genetic vulnerability might play an important role in such instances.

### Drug Accumulation

Drug accumulation can take place when the drug is reintroduced too early, that being before the equivalent quantity of the previous dose has been eliminated causing an increase in plasma concentration leading to possible toxic phenomena due to accumulation. Accumulation is thus inversely proportional to the percentage of the dosage eliminated between administrations.

Drug accumulation can also take place because of a reduced elimination of the drug (i.e. patients with a kidney failure condition) or because of a pathologic state which slows down the hepatic and extra-hepatic metabolic processes. Co-administration of drugs can also cause accumulation as mentioned above because of either pharmaco-dynamic or pharmaco-kinetic interferences. Finally, we can observe accumulation when using drugs with a slow elimination rate and/or a longer half-life, either because of the slowness in reaching equilibrium or in the decrease of plasma concentration once the therapy is suspended[2].

In our otoaudiologic field we experience this problem because of the age group our patients fall into and because of the often chronic audio-vestibular conditions we treat. As a matter of fact we often treat older patients suffering from other conditions and following other pharmacological treatments, especially the ones with chronic pathologies.

Elderly patients must use extreme caution using drugs because they often have to use a number of different drugs, increasing the risk of interactions and adverse reactions. They tend to have a slower metabolism so food and drugs are eliminated at a slower rate; consequently drugs tend to remain in their system for a longer period of time creating accumulation. The nervous system becomes more sensitive with age and many common drugs like opioid analgesics, benzodiazepine, anti-psychotics, Parkinson's disease drugs have to be used with caution. In a similar way other organs could be more reactive to certain molecules i.e. non-steroidal anti-hypertensive or anti-inflammatory drugs. The reasons above are why elderly patients are more sensitive to side affects and tend to accumulate massive amounts of drugs in their system.

There is also a need to consider other factors like self-medication, very common among the elderly who often use drugs unnecessarily or don't seek medical advice, either because of lack of knowledge or just carelessness, and other age-related factors like loss of memory, eyesight and manual dexterity which can all interfere with a proper drug administration schedule.

### Pharmaceutical Drugs: Pre-marketing Studies

Before a new medication is released on the market and prescribed to people, it needs to be proved safe, active and effective and that the relation between the risk of side effects and therapeutic benefits is beneficial. The owner of the medication, normally the pharmaceutical company, is responsible for collecting all of this information. Developing a new medication normally takes a long period of time, sometimes a few years, in pre-clinical laboratory studies on animals and clinical studies on humans.

Agencies like the Food and Drugs Administration (FDA) in the USA and the European Medicines Agency (EMEA) in the EU rule pharmaceutical research. The Italian Medicines Agency (AIFA) was recently established in Italy. Studies on both animals and humans have to be submitted to these agencies in order to obtain approval for market release and for clinical use.

In 1970 the British Committee on the Safety of Drugs (today called Committee on Safety of Medicines) stated in its annual report[4] "it is well known that a medication that is effective involves a number of risks. Furthermore it is not certain that all risks can be identified before its release to the public, not all trials on animals and humans will reveal all the possible side-effects of a medication. This data will only be available after a medication has been administered to a large number of patients over a long period of time".

It has recently been determined[5] that 51 percent of the approved drugs show severe adverse reactions undetected before approval.

Adverse Drug Reactions (ADRs) can thus be identified either before or after the experimental phases that lead to final market release. Pre-marketing clinical trials seldom identify or determine the frequency of severe adverse reactions. The information sheet of the medication states the information available at the time of approval. The result of this process is that once the medication is released on the market both doctor and patient are often unaware that they are continuing to test the drug even to a much greater level than the experiments previously done.

### Drug Safety Monitoring

Drug safety monitoring is the process of evaluating the undesirable side effects potentially related to the pharmacologic treatment[6].

Drug safety monitoring has four main objectives[7]:

- To detect new ADRs as soon as possible.
- To improve and distribute information regarding known or suspected ADRs.
- To evaluate the advantages of a medication versus another or over other types of therapy.
- To provide information in order to improve medical practices.

Most common ADRs are severe and related to new drugs released on the market[8].

The main effects observed[8,9] are related to the gastro enteric system (31-35%), central nervous system (15-20%), and skin (10-11%).

The most common drugs[8,9] causing ADRs are the cardiovascular ones.

### ADR Classification and Definition

Adverse reactions to medication have different forms, are heterogeneous and often unexpected and unpredicted[10].

They can be classified, as per the Inman[11] proposal, in three types A, B and C depending on their characteristics, on the difficulty of identification and on the most effective methods to identify them[12].

ADRs of the A type are the most common ones and are defined by the World Health Organisation (WHO) as side effects. They tend to be fairly common and dosage-related. They can be caused by an excessive pharmacological action or by a secondary pharmacological action of the medication or even by pharmaco-kinetic interferences. Even though their incidence and morbidity is high they seldom cause a threat to the patient's life. They can normally be detected before market release and can be replicated in the laboratory. Nevertheless, their identification can be more complex under certain conditions like: when only a minority of the subjects show a reaction, or when there isn't a direct relation with dosage, or when the reaction is common or not important, or when it is difficult to obtain on animals, or when they coincide with other causes (e.g. cephalalgia). The mechanism is unclear.

ADRs of the B type are often of an allergic, immunologic or idiosyncratic nature and take place in a minority of patients (less than 1 per 1000) and they are normally unexpected and unpredictable. They are generally severe and have little or no relation to dosage, they don't represent an extension of the pharmacological reaction and are difficult to identify for a number of reasons. They tend to affect certain organs: liver, hematopoietic system and skin. The time frame between the medication intake and the appearance of the symptoms and the low retrospective frequency of the symptoms lead to consider the medication responsible for the reaction. Except for conditions of immediate hypersensitivity (anaphylaxis) these reactions take place normally after five days from beginning of the treatment (time in which cells become hyper-sensitive to the drug) and there is no upper limit even though most reactions take place within the first twelve weeks.

Patients often have predispositions that are not always evident. Certain reactions have an immunological base, others recognise a metabolic genetic error or an acquired deficiency to a certain enzyme, causing an abnormal metabolic pathway or an accumulation of toxic metabolites.

Regarding type C ADRs we need to say that, especially when medication is used over many years or for the rest of one's life, they can induce new medical conditions or change the incidence of the existing ones. Examples of this risk can be identified with the possible incidence of breast cancer or thromboembolic complications induced by birth control pills. These events can be severe and fairly common and can significantly affect public health. The late onset of a disease makes it difficult to identify it as a pharmaco-related pathology.

ADRs regarding our field can definitely be attributed to the first group, type A. They are in fact undesired effects, common type, dosage related and non-life threatening.

Specifically, ototoxicity is regarded as an adverse reaction affecting the inner ear leading to alterations either transitory or permanent of the auditory or vestibular functions. We believe that research over the last decades on the suspected drugs action mechanisms still has a long way to go. It is then very important to gain a deeper knowledge of these action mechanisms in the future in order to let the patient benefit from the most effective means of prevention derived from therapy[13]. Complete or partial loss of the auditory or vestibular functions can have a severe impact on quality of life and socioeconomic status[14].

### Incidence and Frequency of ADRs

Evaluating the incidence and frequency of ADRs is not simple because the comparison between published studies is not always possible due to the differences in exposition to the specific drug of different populations or the differences in the ADR detection methods. In fact, some studies only account for adverse reactions while others also account for overdose or because certain studies consider only the manifested clinical conditions and others consider laboratory parameter alterations as well[15-29].

ADRs are responsible for 3-7% of all hospitalisation cases. The U.S. prospective studies showed ADRs in 10-20% of all hospitalisations, in which 10-20% were severe. The incidence of death caused by ADRs is unknown, they suggested rates between 0.5 and 0.9% but they included patients with complex and severe pathologies[20,21,23-29].

Incidence and severity of ADRs can be influenced by many factors related to the patient (age, gender, present diseases, genetic factors and geographic factors) and to the medication (type of drug, route of administration, therapy duration, dosage and bio-availability). Incidence and severity are probably higher in older people. It is unclear how prescription errors and patients lack of compliance affect ADR incidence.

Pharmaceutical producers declare the frequency of side effect occurrences on certain medications. Such information is reported through a grading system going from < 0,01% (very rare) to >=10% (very common).

Nowadays, drug safety surveillance institutions tend to persuade the pharmaceutical industry to improve the utilisation of this grading scale as a main element in the general management of the pharmacological therapy.

Because of this, the data we now hold will soon be updated and become more detailed.

### ADR Costs

Adverse reactions do not only affect people's health but have a great economic impact as well.

The research on ADR costs has only recently started, following the Institutions request to reduce public health costs.

Works published in the last years have tried to quantify costs and research had to be based on factors like the increase in incidence on medical exams, the number of hospitalisations, the number of additional therapies needed and the lengthening of hospitalisation periods, etc[18,24,27,30,31].

### Ototoxicity

Let's now make a few considerations on ototoxicity without expecting them to be exhaustive on such a complex and articulated topic that in many ways is still unknown.

Ototoxicity is defined by the toxic capacity of certain drugs or toxins relative to the inner ear structures (particularly to the cochlea and the vestibular cells) or the acoustic nerve. Ototoxic drugs can act on the cochlea, the vestibular system or both[32-34].

Toxic damage is often shown by symptoms like tinnitus, vertigo, hyperacusis and deafness. Hearing impairment, tinnitus and vertigo are the most important medical conditions of the inner ear due to a drug-induced damage. The onset of these symptoms can be simultaneous or singular, they can develop rapidly or gradually and can be reversible or not. The ototoxic action can lead, in the most severe cases, to remarkable functional reductions of the hearing capability or complete deafness[32-33-34].

A possible genetic predisposition is assumed to be facilitating the ototoxic action[35-40]. There is a remarkable difference in ototoxic sensitivity among different animal species. This information has to be carefully taken into consideration when translating research from animal models to humans[41]. As an example, guinea pigs and humans share the same ototoxic dosage of cisplatin, while guinea pigs showed much more tolerant to gentamicin than humans[41]. These drugs can be dangerous for both the auditory and the vestibular parts and to a greater extent to the organ of Corti (cochleotoxic).

Because almost every ototoxic drug is eliminated through the kidneys the reaching of levels of toxicity is facilitated by renal failure. Whenever the renal function is altered ototoxic drug dosages, eliminated through the kidneys, have to be corrected so that hematic levels remain within therapeutic limits. Serum levels of the drug (high or minimal) should be checked in order to get the correct therapeutical levels. As a matter of fact even with subjective changes of sensitivity to the drug, hearing is usually preserved if hematic levels remain within the suggested limits.

Ototoxic drugs shouldn't be prescribed for topical medications in the event of an eardrum perforation since the inner ear fluids, through the secondary eardrum of the oval window, could absorb the drug. This practice is quite debated but it is fairly common to find a clinical usage of eardrops containing antibiotics or other ototoxic drugs in chronic otitis even in the presence of a perforated eardrum[42,43].

Ototoxic antibiotics should not be used on pregnant women. Hearing impaired and elderly people should not be given ototoxic medications if a non-toxic alternative is available. An evaluation of a pre-existing condition of hearing impairment should be done before prescribing ototoxic antibiotics. Hearing ability has to be monitored through audiometric exams throughout the therapy. According to the American Speech-Language-Hearing Association (ASHA) a tonal audiometric exam should be carried out 24 hours after the beginning of the therapy and every two or three days for the rest of the therapy.

The high frequency analysis would supply even more precise and reliable results[44-47].

The reason for this monitoring is to obtain a physio-pathological description of the ototoxic agents derived damages, outlining the clinical aspects of the damages to the cochlea and to the vestibular receptors, keeping track of the changes over time[48]. High frequencies are generally more sensitive to the treatment and high-pitched tinnitus or vertigo can take place, but they are not always reliable signs to pre-alert.

Transient evoked otoacoustic emission (TEOAE) and distortion product otoacoustic emission (DPOAE) tests are today considered gold-standard exams in ototoxicity control, allowing assessment of cochlea function at high frequencies in just a few minutes. Clinical studies confirm the strict relationship between otoemission and ototoxicity. Otoemissions as a matter of fact allow the detection of levels of ototoxicity from the beginning of the treatment, sometimes even before any audiometric deficit is detected.

The simultaneous exposition to noise is a worsening factor due to the increased release of free radicals.

Cochlear dysfunction can span from a light increase of the hearing threshold, only detectable through audiometry, to complete deafness. Hearing loss can take place along with either temporary or permanent tinnitus. Clinically cochlear damage appears sooner than vestibular damage that could even be severe before the onset of vertigo. The actual extent of vestibular damage is hard to assess, vestibular damages can go undetected especially if the damage development is slow and progressive (in most cases bilateral)[47].

Early detection of toxicity enables the adjustment of dosage, the suspension of therapy and the change of medication. In many instances damage evolves over time: in a group of paediatric patients, damage of 11% at the beginning of treatment increased to 44% two years later[49].

Ototoxicity is considered a pharmacological adverse reaction affecting the inner ear, characterized by cochlear or vestibular dysfunction.

The Council for International Organisations of Medical Sciences (CMIOS), in order to standardise the terminology regarding medication safety, has produced a list of definitions of ADRs and the relative proper procedures. The developments of deafness, tinnitus or vertigo associated with pharmacological treatment are minimum requirements to refer to ADRs.

While an ototoxic damage can be determined by a routine anamnesis, ototoxic loss of hearing can only be determined by comparison of audiograms from before and after the treatment. To diagnose a pharmacologically caused deafness it is necessary to verify through audiometry an increase of the equal loudness contour by 15dB over one or more frequencies. In any case it is hard to mention pharmacological etiology without having audiograms from before and after the therapy.

Legal debates over iatrogenic damage due to ototoxicity are very rare and only attaining severe cases that led to communication disorders (severe hearing loss over many frequencies)[48].

Drugs ototoxicity is a very delicate issue because many pathologies are treated through the use of drugs that are potentially harmful to the inner ear.

There is evidence about inner ear tissues being immunologically, biochemically and functionally related to kidney tissues. It seems that medications affecting sodium and potassium transport alter ionic homeostasis of the inner ear causing functional problems like hearing loss, tinnitus and vertigo[44]. Renal pharmacological adverse reactions have been studied in the effort of finding predictive signs of possible ADRs related to the inner ear or to the labyrinth and about medication class's influence upon ionic transportation. Resulting data showed that renal ADRs couldn't be considered markers of pharmacologically induced disturbances to the inner ear or labyrinth. Nevertheless, the ability of these drugs to influence the ion transport system and the ion channels and so influencing the ear and kidney ionic homeostasis could be a predicting factor for a possible pharmaceutical related ototoxicity[44].

No dosage appears to be safe in amino-glycoside therapies no matter what the administration route is (parenteral, intratympanic, per os, intrathecal). Certain studies show how a daily single administration of amino-glycosides is as effective as a set of daily injections, thus a smaller quantity of the medication leads to the same results[50].

In any case monitoring the cochleo-vestibular function is always very important. Genetic predisposition has been suspected for severe deafness onsets just after a few amino-glycoside injections. As far as medication interactions are concerned, specifically between amino-glycosides and other drugs, the issue has been covered in the preceding paragraph (see page 602, Interactions).

Individual susceptibility and organ vulnerability are debated issues because of their relevance and criticality and often related to genetic characteristics. Several studies today reveal how certain mitochondrial chromosome mutations can represent one of the genetic factors for hypersensitivity, vulnerability and predisposition towards amino-glycosides[51-53].

A hereditary non-syndromic familiar form associated with the A1555G mutation (substitution of a guanine with an adenine) located on the mitochondrial RNA12S has been discovered[51]. The A1555G mutation is very common in Spain, reaching 25%[45]. Due to the high incidence in this country, detection of the genetic mutation is carried out systematically in order to avoid amino-glycoside ototoxicity[51,54-57].

Bacteric ribosomal RNA is the amino-glycosides target and the mutated human form A1555G is very similar to the bacteric one, it binds abnormally to the amino-glycoside explaining the reason for deafness even at low dosages of the drug. Some authors report that 17% of the subjects interested by amino-glycoside ototoxic effects have such mutation[51-53,58].

A recent study on the frequency of mitochondric mutation over a selected Japanese population specifically selected because had experienced post-streptomycin tinnitus has shown the possibility that a new and rare mutation, C1556T, could appear along with the A1555G as a hearing loss risk factor, specifically as a tinnitus-generating factor. It must be noted that according to the available literature the A1555G mutation doesn't create any vulnerability of the vestibular apparatus even though the chromosomal mutation is present in all mitochondria of every tissue. The C1494T is another 12S ribosomal RNA mutation that can cause even if to a lesser degree amino-glycoside susceptibility[59].

We have seen that the way cisplatin causes ototoxicity varies significantly from subject to subject and that it is partially related to the genetic differences of the subjects[39].

Identifying genetic variations and so predicting the severity of ototoxic effects would be an important step towards a better-addressed use of cisplatin[39].

## Guide Presentation

This work on ototoxic, tinnitus and vertigo-generating medications is, an update and a revision of the previous guide published in 2005, regarding collateral and undesired effects of medications in the oto-audiologic field[1]. We have adjusted the Italian pharmacological context, regarding active principles, to the international Anglo-Saxon one, intentionally omitting in this review commercial products as they pertain to individual country contexts.

This guide should be a practical, comprehensive list of drugs (actually of the active principles of the drugs) used in this country and yet known and used abroad, which can induce otologic and otoneurologic side effects, such as:

**1.** Ototoxicity, as a neurosensorial hearing damage also including the possible associated labirintine vertigo symptomatology and/or the possible onset of tinnitus;

**2.** The onset of tinnitus only, with no documentable hearing damage;
**3.** The vertigo generating action only, without any evident toxic action on the hearing apparatus.

These side effects have a different weight from a practical point of view. In fact, while adverse reactions related to ototoxicity can justify higher levels of alert based on the ADR scale according to Hartwig et al[60], side effect-generating tinnitus and vertigo hold a certainly lower level of gravity.

Data contained in publication is a complex elaboration of the information found on the "Guida all'uso dei Farmaci" (2008), based on the British National Formulary (BNF), by the Italian Department of Health and by the Italian Medicines Agency (AIFA).

The Guide mentioned is a translation and an adaptation to the Italian context of the British National Formulary, a prestigious publication created in Great Britain many years ago and made possible thanks to a scientific collaboration agreement between AIFA, the British Medical Association and the Royal Pharmaceutical Society of Great Britain.

The Drugs User's Guide is an easy to access manual, where the most relevant information regarding the active principals of the drugs on our market are gathered. It gives reference to the conditions for which they are suggested and valuable indications for prescriptions to categories of patients particularly subject to the risk of undesired reactions like elderly people, children and subjects with severe chronic conditions who require co-administration of more drugs.

For this reason we believe it to be a useful contribution to professionals in this field.

### *Work Plan and Hints for Directory Consultation*

In this work the list of the pharmacological active principles is divided into sub-categories based on the type of audiologic and otoneurologic side effects (hearing losses and disturbances, tinnitus, balance disorders and vertigo) reported by the pharmaceutical companies and/or by the Health Department directives (the type of side effect is indicated in our lists with a number from 1 to 4).

Whenever possible we kept in consideration the classification of drugs based on the apparatus they attain to, the therapeutic indications and the pharmaco-clinical actions and we made alphabetical lists for easy reference.

More specifically these are the various types of side effects listed and numbered:

**1.** Drugs with the explicit indication, by the pharmaceutical company and/or the Health Department, of "potentially otologically harmful", generally indicated as ototoxicity (ototoxic drugs); ototoxicity is meant as a neurosensorial hearing damage (going from light hearing impairment to deafness) and may include both the possible associated symptomatology of labyrinthical alteration vertigo and the possible generation of tinnitus;
**2.** Drugs with the explicit indication, by the pharmaceutical company and/or the Health Department, as potentially tinnitus-generating, generally called tinnitus, hissing ear, or acouphene (drugs openly declared as tinnitus generating); a potential tinnitus risk is reported for these drugs and there is no mention of ototoxicity;
**3.** Drugs with the explicit indication, by the pharmaceutical company and/or the Health Department, as potentially vertigo-generating drugs, generally called vertigo or dizziness (drugs openly declared as vertigo generating). Information of potential vertigo associated with the drug is reported while there is no mention of ototoxicity;
**4.** Drugs with possible audiologic effects, indicated as "hearing disturbances" (drugs with aspecific otologic side effects), it is advisable to have a conservative approach to these drugs and to evaluate in each case the possible intensity and type of adverse reaction.

Certain drugs can clearly be found in more than one sub-category as they can lead to different ENT interests.

In order to provide an easier and better reference, active principles in this book have been grouped and listed in different ways:

**Index A**: general index, where we find the active principles sorted mainly in reference to the apparatus they act upon, to the generic indications and to the pharmaco-clinical action and with a reference to the relevant side effect, using the grading scale 1 to 4 mentioned above. We literally reproduced the "Guida all'uso dei Farmaci" (2008) layout to facilitate consultation.
**Sub-indexes A1-A2-A3-A4:** the pharmacological active principles have been divided into four side affect categories while maintaining the same order of index A, by apparatuses, clinical indications and pharmaco-clinical actions.

**Index B:** in this index the active principles are listed in alphabetical order, each with a numerical reference to the relevant type of side effect. Whenever possible according to data available to us, believing it to be very useful, we indicated the side effect frequency for each drug using a grading scale from *a* to *e* going from "very common" to "very rare".

Pharmaceutical company indications about side effect frequency are normally expressed as follows:

**a** Very common (≥ 10%)
**b** Common (≥ 1% e < 10%)
**c** Uncommon (≥ 0,1% e <1%)
**d** Rare ( ≥ 0,01% e < 0,1%)
**e** Very rare (< 0,01%)
**f** Unknown, because available data is insufficient

It must be said that this grading is sometimes not published or known by the manufacturers so we haven't assigned a grading letter to drugs with missing data.

## Final Considerations and Behavioural Strategies for Practitioners

Based upon what was said so far, the suggested behaviour for General Practitioners or for ENT/Audiology specialists, whenever they should encounter problems connected to potentially risky pharmacological treatments, cannot be as univocal, peremptory and directional.

As we mentioned in the foreword, the practitioner must always have the objective of finding the right balance between effectiveness and safety keeping in mind that pharmacological programming optimisation also means obtaining a reasonable compromise between clinical advantages and risks related to adverse or undesired side effects.

For this reason it is impossible to generalise the strategies a practitioner has to follow. Instead every patient needs to be studied transversally and observed longitudinally in an absolutely elastic and individualistic way.

In each case the coexistence of additional risk factors like old age, kidney conditions, dysmetabolic conditions, environmentally-related conditions of exposition to noise, genetic or familiar predisposition to auditory pathologies or the coexistence of non-iatrogenic neuro-sensorial audiologic pathologies are all elements which could interfere with iatrogenic factors increasing the risk for ADRs.

The following suggestions may be given:

**1.** During anamnesis the pharmaco-therapeutic profile of the patient accurately mark, previous, current and scheduled intakes of drugs with potential risk of ADR, making note of the molecule, the commercial name, the posology, length of treatment and type of ADR and other possible additional and collateral factors of risk.

**2.** When dealing with a life-saving treatment or a treatment that cannot be stopped and/or is a result of a long series of therapeutic trials, it is improper to operate or to advise the patient's doctor for any changes of the therapeutic profile, generating unnecessary fears in the patient. This is valid if we face an ototoxic drug treatment or, even more, if we deal only with tinnitus and/or vertigo inducing drugs.
We have to be reassuring with the patient and warn him (in line with the current prescriptions of the law and with the professional advises on using proper care about the patient's consent, when the treatment involves the use of ototoxic drugs) that possible disturbances could be a normal consequence of the important treatment the patient is undergoing. The patient must also be informed that the disturbances will be strictly monitored and that will be softened by cell protecting treatments and/or small dosage adjustments.
This soft, minimizing yet directional approach could reveal very useful with patients showing tinnitus as a central symptom, whose psychological involvement is well known to be frequent and penetrating.

**3.** The doctor's behaviour towards patients whose pathologies are less severe and where medication can be modified on both posology and type, is definitely different. In such cases, if using ototoxic drugs, it is possible to act before irreversible alterations take place, by talking to the patient's doctor and trying to co-manage the case by small therapeutic adjustments or more radical changes of the pharmacological profile. When dealing with non ototoxic tinnitus and or vertigo inducing drugs and in presence of a symptomatology, and the relationship the drug intake and the sympto-

matology being unclear, it is possible with a dechallenge/rechallenge strategy either partial or total depending on the case.
Since harmful consequences for the auditory system cannot be predictable when using non-ototoxic drugs, there is wider flexibility regarding the medical and legal information to be given to the patient.

**4.** While managing different strategies it is advisable to keep in consideration the concept of frequency (very common-very rare) of side effects, at least for those drugs for which data is available; such element, which we classified with the "a, b, c, d, e" codes, might reveal useful and sometimes determinant when choosing the strategic behaviour to be adopted by the ENT/Audiology Specialist

**5.** With the current knowledge to this date, it is impossible to advise the patient's doctor and the specialist on behavioural strategies when dealing with drugs of category 4 ("hearing disturbances") because the data available is very limited on frequency and none on the specific type of side effect.
In such instances, especially with drugs with ADR's rated "common" or "very common", the only advise that could be given is to be cautious.
We can finally say that a reasonable use of the drug, including the early identification of the minimum effective dose, is certainly the best way to reduce ototoxicity incidence.
A better diffusion of the monitoring techniques would be useful even though they are still quite unknown today and rarely requested. Although ototoxic phenomena incidence is underestimated, identifying subjects with risk of genetic predisposition and reducing self-medication instances along with a proper policy on the patient's drug use education will certainly help narrowing the number of ototoxicity cases.
The Specialist is ultimately responsible for diagnosis, medical care, giving advise, prevention and rehabilitation when dealing with the effects of medications on the inner ear.

## Conclusions

This work represents the update and the revision of the previous guide on the unwanted side effects in the oto-audiological field. We believe it has a larger international value and is to be considered useful to any physician regardless of the country he/she operates in.

The risk of drug side-effects has become a burning issue, therefore, in daily clinical practice, doctors need to focus in that direction also in consideration of the possible medical-legal implications.

It will be useful and necessary to periodically update the data of the guide on the basis of the new acquisitions about drugs. Obviously, in the pharmacological scene of each country, there might be some drugs which are not included in the above mentioned list or, on the contrary, some of the drugs listed here might not be included in those used in some countries.

The general interest of this document survives, as it may provide a pratical and useful guide for physicians in their daily professional activity.

## Index A

General index, where we find the active principles sorted mainly in reference to the apparatus they act upon, to the generic indications and to the pharmaco-clinical action and with a reference to the relevant side effect, using the grading scale 1 to 4 mentioned above:

**1.** Ototoxic drugs (ototoxicity may include both the possible associated symptomatology of labyrinthical alteration vertigo and the possible generation of tinnitus);

**2.** Drugs tinnitus-generating (there is no mention of ototoxicity);

**3.** Drugs vertigo-generating (there is no mention of ototoxicity);

**4.** Drugs with possible audiologic effects, indicated as "hearing disturbances" (drugs with aspecific otologic side effects).

### Gastrointestinal System

*Antispasmotic and other drugs used for intestinal motility disorders*

- Antimuscarinic
  - Butylscopolamine bromide . . . . . 3
  - Propantheline bromide . . . . . 3
  - Sulphate atropine . . . . . 3

*Antisecretory and protective drugs on gastric mucosa*

- H2 blockers
  - Cimetidine . . . . . 3

- – Famotidine . . . . . 3
- – Nizatidine . . . . . 3
- – Ranitidine . . . . . 3

• Chelates and complexes
- – Sucralfate . . . . . 3

• Prostaglandins analogues
- – Misoprostol . . . . . 3

• Proton pump inhibitors
- – Esomeprazole . . . . . 3
- – Lansoprazole . . . . . 3
- – Omeprazole . . . . . 3
- – Pantoprazole . . . . . 3
- – Rabeprazole sodium . . . . . 3

*Anti-diarrheal drugs*

• Gastrointestinal motility inhibitors
- – Loperamide hydrochloride . . . . . 3

*Chronic intestinal disorders*

• Aminosalicylates
- – Sulfasalazine . . . . . 2,3

• Cytokines inhibitors
- – Infliximab . . . . . 3

## Cardiovascular System

*Positive inotropes*

• Cardiac glycoside
- – Digitoxin . . . . . 3
- – Digoxin . . . . . 3

*Diuretics*

• Thiazide and related diuretics
- – Chlorthalidone . . . . . 3
- – Hydrochlorotiazide . . . . . 3
- – Indapamide . . . . . 3

• Loop diuretics
- – Furosemide . . . . . 1
- – Torsemide (usually in high and rapid parenteral administration and in renal failure) . . . . . 1

• Potassium-sparing and other diuretics
- – Amiloride and hydrochlorothiazide . . . . . 2,3

*Anti-arrhythmics*

• Supraventricular and ventricular arrhythmias
- – Amiodarone hydrochloride . . . . . 3
- – Flecainide acetate . . . . . 2,3
- – Propafenone hydrochloride . . . . . 3

• Ventricular arrhythmias
- – Mexiletine hydrochloride . . . . . 3

*Beta blockers*
- – Acebutolol . . . . . 3
- – Atenolol . . . . . 3
- – Atenolol + diuretics . . . . . 3
- – Atenolol + calcium channel blockers . . . . . 3
- – Bisoprolol fumarate . . . . . 3
- – Bisoprolol fumarate + diuretics . . . . . 3
- – Carvedilol . . . . . 3
- – Celiprolol hydrochloride . . . . . 3
- – Esmolol hydrochloride . . . . . 3
- – Metoprolol tartrate . . . . . 3
- – Metoprolol + diuretics . . . . . 3
- – Nadolol . . . . . 3
- – Nebivolol . . . . . 3
- – Oxprenolol + diuretics . . . . . 3
- – Pindolol . . . . . 3
- – Propranolol hydrochloride . . . . . 3
- – Sotalol hydrochloride . . . . . 3
- – Timolol maleate . . . . . 2,3

*Hypertension and heart failure*

• Anti-hypertensive vasodilators
- – Sildenafil . . . . . 3
- – Sodium nitroprusside (related with rapid reduction of blood pressure) . . . . . 3

• Centrally-acting anti-hypertensive drugs
- – Clonidine hydrochloride . . . . . 3
- – Methyl dopa . . . . . 3
- – Moxonidina . . . . . 3

• Alpha blockers
- – Doxazosin . . . . . 3
- – Terazosin . . . . . 3

• Drugs used for regulate renin-angiotensin system
- – Ace inhibitors
  - Captopril . . . . . 3
  - Captopril + diuretics . . . . . 3
  - Cilazapril . . . . . 3
  - Cilazapril + diuretics . . . . . .3
  - Enalapril maleate . . . . . 2,3
  - Enalapril + diuretics . . . . . 2,3
  - Fosinopril . . . . . 3
  - Fosinopril + diuretics . . . . . 3
  - Lisinopril . . . . . 3
  - Lisinopril + diuretics . . . . . 3
  - Moexipril hydrochloride . . . . . 2,3
  - Moexipril + diuretics . . . . . 2,3
  - Perindopril . . . . . 3
  - Perindopril + diuretics . . . . . 3
  - Quinapril . . . . . 3
  - Quinapril+diuretics . . . . . 3
  - Ramipril . . . . . 3
  - Ramipril+diuretics . . . . . 3
  - Trandolapril . . . . . 3
  - Trandolapril + calcium channel blockers . . . . 3
- – Angiotensin II receptor blockers
  - Candesartan cilexetil . . . . . 3
  - Candesartan + diuretics . . . . . 3
  - Eprosartan . . . . . 3
  - Irbesartan . . . . . 2
  - Irbesartan+diuretics . . . . . 2,3
  - Losartan potassium . . . . . 3
  - Losartan potassium+diuretic . . . . . 3
  - Olmesartan medoxomil . . . . . 3
  - Olmesartan medoxomil+diuretics . . . . . 3
  - Telmisartan . . . . . 3
  - Telmisartan + diuretics . . . . . 3
  - Valsartan + diuretics . . . . . 2,3

• Nitrates, calcium channel blockers and other drugs used for angina
- – Nitrates
  - Nitroglycerin . . . . . 3
  - Isosorbide dinitrate . . . . . 3

Isosorbide mononitrate . . . . . 3
– Calcium channel blockers
Amlodipine . . . . . 2,3
Diltiazem hydrochloride . . . . . 3
Felodipine . . . . . 3
Isradipine . . . . . 3
Lacidipine . . . . . 3
Lercanidipine hydrochloride . . . . . 3
Nicardipine hydrochloride . . . . . 2,3
Nifedipine . . . . . 3
Nifedipine + atenolol . . . . . 3
Nisoldipine . . . . . 3
Verapamil hydrochloride . . . . . 3
• Peripheral vasodilators and related drugs
– Pentoxifylline . . . . . 3
*Sympathomimetics*
• Cardiopulmonary resuscitation
– Adrenaline . . . . . 3
*Parenteral anticoagulants*
– Fondaparinux . . . . . 3
*Anti-platelet agents*
– Clopidogrel bisulfate . . . . . 3
– Dipyridamole . . . . . 3
*Anti-fibrinolytic and hemostatic drugs*
– Tranexamic acid (in rapid intravenous injection) . . . . . 3
*Blood derivatives*
– Human coagulation factor VIII . . . . . 3
– Human coagulation factor IX . . . . . 3
*Lipid – lowering medications*
• Fibrates
– Bezafibrate . . . . . 3
– Fenofibrate . . . . . 3
– Gemfibrozil . . . . . 3
• Statins
– Atorvastatin . . . . . 2,3
– Pravastatin sodium . . . . . 3
– Rosuvastatin . . . . . .3
– Simvastatin . . . . . 3
– Simvastatin + ezetimibe . . . . . 3
• Fish oil
– Omega-3 acid ethyl esters . . . . . 3

## Respiratory System

*Drugs used in asthma and chronic obstructive pulmonary disease*
• Adrenergic receptor agonists (sympathomimetics)
– Beta 2 selective agonists
Salmeterol . . . . . 3
• Antimuscarinic bronchodilators
– Tiotropium . . . . . 3
*Cromoglycate, related therapies and anti-leukotrienes*
• Anti-leukotrienes
• Montelukast . . . . . 3
*Antihistamines and drugs used for alleric reactions*
• Sedative antihistamines
– Chlorpheniramine maleate . . . . . 2
– Ketotifen . . . . . 3
• Allergen immunotherapy
– Omalizumab . . . . . 3

## Central Nervous System

*Hypnotic and anxiolytic drugs*
• Hypnotics
– Benzodiazepines
Diazepam . . . . . 3
Flurazepam . . . . . 3
Lormetazepam . . . . . 3
Nitrazepam . . . . . 3
Temazepam . . . . . 3
– Zaleplon, zolpidem e zopiclone
Zaleplon . . . . . 3,4
Zolpidem tartrate . . . . . 3,4
Zopiclone . . . . . 3
– Sodium oxybate
Sodium oxybate . . . . . 3
• Anxiolytics
– Benzodiazepines . . . . . .
Alprazolam . . . . . 3
Chlordiazepoxide . . . . . 3
Diazepam . . . . . 3
Lorazepam . . . . . 3
Oxazepam . . . . . 3
– Buspirone
Buspirone hydrochloride . . . . . 3
– Meprobamate
Meprobamate . . . . . 3
*Barbiturates*
• Phenobarbital . . . . . 3
*Drugs used for psychosis and related disorders*
• Atypical antipsychotics
– Amisulpride . . . . . 3
– Aripiprazole . . . . . 3
– Clorazepate dipotassium . . . . . 3
– Olanzapine . . . . . 3
– Quetiapine . . . . . 3
– Risperidone . . . . . 3
*Antidepressants*
• Tricyclic antidepressants and related drugs
– Tricyclic antidepressant
Amitriptyline hydrochloride . . . . . 2,3
Amitriptyline hydrochloride + perphenazine . . 2,3
Clomipramine hydrochloride . . . . . 2,3
Dosulepin hydrochloride . . . . . 2,3
Imipramine hydrochloride . . . . . 2,3
Nortriptyline . . . . . 2,3
Fluphenazine/nortriptyline . . . . . 2,3
Trimipramine . . . . . 2,3
– Related antidepressant
Mianserin hydrochloride . . . . . 2,3
Trazodone hydrochloride . . . . . 2,3
• Selective serotonin reuptake inhibitors
– Citalopram . . . . . 2,3
– Escitalopram . . . . . 3
– Fluoxetine . . . . . 3

- – Fluvoxamine maleate . . . . . 3
- – Paroxetine . . . . . 3
- – Sertraline . . . . . 3
- • Other antidepressants
- – Duloxetine . . . . . 3
- – Mirtazapine . . . . . 3
- – Reboxetine . . . . . 3
- – Venlafaxine . . . . . 2,3

*Central nervous system stimulants and drugs used for attention deficit disorders and hyperactivity*

- • Atomoxetine . . . . . 3
- • Metilphenidate hydrochloride . . . . . 3
- • Modafinil . . . . . 3

*Drugs used in nausea and vertigo*

- • Serotonin antagonists (5-ht3 receptor antagonists)
- – Dolasetron mesylate . . . . . 3
- – Ondansetron . . . . . 3
- – Palonosetron . . . . . 2,3
- – Tropisetron . . . . . 3
- • Neurokinin receptor antagonists
- – Aprepitant . . . . . 2,3
- • Scopolamine
- – Scopolamine hydrobromide . . . . . 3

*Analgesics*

- • Non opioid analgesic
- – Acetylsalicylic acid . . . . . 1
- – Paracetamol + codeine phosphate . . . . . 3
- • Opioid analgesics
- – Buprenorphine . . . . . 2,3
- – Fentanyl . . . . . 3
- – Methadone hydrochloride . . . . . 3
- – Morphine . . . . . 3
- – Oxycodone hydrochloride . . . . . 3
- – Pentazocine . . . . . 3
- – Pethidine hydrochloride . . . . . 3
- – Tramadol . . . . . 3
- • Neuropathic pain (trigeminal neuralgia)
- – Carbamazepine . . . . . 3
- – Oxcarbazepine . . . . . 3
- • Anti migraine drugs
- • Migraine acute treatment
- – Acetylsalicylic acid . . . . . 1
- – NSAIDs . . . . . 2,3
- • 5-hydroxy tryptamine agonists
- – Almotriptan . . . . . 2,3
- – Eletriptan . . . . . 2,3
- – Frovatriptan . . . . . 2,3
- – Rizatriptan . . . . . 3
- – Sumatriptan . . . . . 3
- – Zolmitriptan . . . . . 3
- • Ergot alkaloids drugs
- – Ergotamine tartrate . . . . . 3
- • Migraine prophylaxis
- – Pizotifen . . . . . 3

*Antiepileptic drugs*

- • Epilepsy control
- – Carbamazepine . . . . . 3
- – Clobazam . . . . . 3
- – Clonazepam . . . . . 3
- – Ethosuximide . . . . . 3
- – Phenytoin . . . . . 3
- – Gabapentin . . . . . 2,3
- – Lamotrigine . . . . . 3
- – Levetiracetam . . . . . 3
- – Oxcarbazepine . . . . . 3
- – Primidone . . . . . 3
- – Pregabalin . . . . . 3,4
- – Tiagabine . . . . . 3
- – Topiramate . . . . . 3
- – Vigabatrin . . . . . 3
- – Zonisamide . . . . . 3
- • Drugs used for status epilepticus
- – Clonazepam . . . . . 3
- – Diazepam . . . . . 3
- – Phenytoin sodium . . . . . 3
- – Lorazepam . . . . . 3

*Parkinsonism and related disorders drugs*

- • Dopaminergic drugs used for parkinsonism
- – Dopamine receptor agonists
  - Cabergoline . . . . . 3
  - Levodopa + benserazide . . . . . 3
  - Levodopa + carbidopa . . . . . 3
  - Levodopa + carbidopa + entacapone . . . . . 3
  - Lisuride maleate . . . . . 3
  - Pergolide . . . . . 3
  - Pramipexole . . . . . 3
  - Ropinirole . . . . . 3
- – Monoamine oxidase b inhibitors
  - Resagiline . . . . . 3
  - Selegiline hydrochloride . . . . . 3
- – Catechol o methyltransferase inhibitors
  - Amantadine hydrochloride . . . . . 3
  - Entacapone . . . . . 3
- – Antimuscarinic drugs used for parkinsonism
  - Orphenadrine hydrochloride . . . . . 3
  - Trihexyphenidyl hydrochloride . . . . . 3
- • Drugs used for essential tremor, corea, tic and related disorders
- – Riluzole . . . . . 3
- • Torsional dystonia and other involuntary movements
- – Botulinum toxin a . . . . . 3

*Drugs addiction*

- • Alcohol dependence
- – Benzodiazepines . . . . . 3
- • Cigarette smoke
- – Bupropion . . . . . 2,3
- – Nicotine drug facts . . . . . 2,3
- – Varenicicline . . . . . 2,3
- • Opioid dependence
- – Buprenorphine . . . . . 2,3
- – Methadone hydrochloride . . . . . 3
- – Naltrexone hydrochloride . . . . . 3
- • Drugs used for dementia
- – Donepezil hydrochloride . . . . . 3
- – Galantamine . . . . . 2,3
- – Memantine hydrochloride . . . . . 3
- – Rivastigmine . . . . . 3

## Infectious Diseases

*Antibiotics*
- Penicillins
  - Broad-spectrum penicillins
    - Amoxycillin + clavulanate . . . . . 3
- Cephalosporins and other beta lactamase
  - Cephalosporins and cephamycins
    - Cefaclor . . . . . 3
    - Cefadroxil . . . . . 3
    - Cephalexin . . . . . 3
    - Cefazolin sodium . . . . . 3
    - Cefixime . . . . . 3
    - Cefotaxime . . . . . 3
    - Cefpodoxime . . . . . 3
    - Cefprozil . . . . . 3
    - Cefradine . . . . . 3
    - Ceftazidime . . . . . 3
    - Ceftriaxone . . . . . 3
    - Cefuroxime . . . . . 3
- Other beta lactamase antibiotics
  - Aztreonam . . . . . 3
  - Ertapenem . . . . . 3
  - Imipenem + cilastatin . . . . . 1
- Tetracyclines
  - Doxycycline . . . . . 2
  - Minocycline . . . . . 1
  - Tigecycline . . . . . 3
- Aminoglycosides
  - Amikacin . . . . . 1
  - Gentamycin . . . . . 1
  - Netilmycin . . . . . 1
  - Tobramycin . . . . . 1
- Macrolides
  - Azithromycin . . . . . 1
  - Clarithromycin . . . . . 1
  - Erythromycin . . . . . 1
  - Telithromycin . . . . . 3
- Other antibiotics
  - Daptomycin . . . . . 3
  - Linezolid . . . . . 2,3
  - Quinupristin + dalfopristin . . . . . 3
  - Teicoplanin . . . . . 1
  - Vancomycin . . . . . 1
- Polymyxin antibiotics
  - Colistin . . . . . 3
- Sulfonamides and trimethoprim
  - Sulfadiazine . . . . . 2,3
  - Sulfamethoxazole + trimethoprim . . . . . 2,3

Antituberculosis drugs
  - Isoniazid . . . . . 3
  - Rifampicin . . . . . 3
  - Rifampicin+isoniazid . . . . . 3
  - Streptomycin . . . . . 1
- Metronidazole and tinidazole . . . . . .
  - Metronidazole . . . . . 3
  - Tinidazole . . . . . 3
- Fluoroquinolones
  - Ciprofloxacin . . . . . 2,3,4
  - Levofloxacin . . . . . 3,4
  - Moxifloxacin . . . . . 3,4
  - Norfloxacin . . . . . 2,3,4
  - Ofloxacin . . . . . 3,4
- Antifungal drugs
  - Amphotericin b . . . . . 1
  - Fluconazole . . . . . 3
  - Flucytosine . . . . . 3
  - Griseofulvin . . . . . 3
  - Itraconazole . . . . . 3
  - Posaconazole . . . . . 3,4
  - Terbinafinae . . . . . 3
  - Voriconazole . . . . . 2,3,4

*Antiviral drugs*
- Human immunodeficiency virus
  - Nucleoside analog reverse transcriptase inhibitors
    - Abacavir . . . . . 3
    - Abacavir+lamivudine . . . . . 3
    - Abacavir+lamivudina+zidovudine . . . . . 3
    - Didanosine . . . . . 3
    - Emtricitabine . . . . . 3
    - Emtricitabine+tenofovir . . . . . 3
    - Lamivudinae . . . . . 3
    - Stavudine . . . . . 3
    - Tenofovir disoproxil . . . . . 3
    - Zidovudine . . . . . 3
    - Zidovudine + lamivudine . . . . . 3
  - Protease inhibitors
    - Atazanavir . . . . . 3
    - Fosamprenavir . . . . . 3
    - Indinavir . . . . . 3
    - Lopinavir+ritonavir . . . . . 3
    - Ritonavir . . . . . 3
    - Saquinavir . . . . . 3
    - Tipranavir . . . . . 3
  - Non-nucleoside reverse transcriptase inhibitors
    - Efavirenz . . . . . 3
  - Other antiretroviral drugs
    - Enfuvirtide . . . . . 3
- Herpes virus infection
  - Herpes simplex and zoster
    - Acyclovir . . . . . 3
    - Famcyclovir . . . . . 3
    - Inosine pranobex . . . . . 3
    - Valacyclovir . . . . . 3
  - Citomegalovirus
    - Foscarnet sodium . . . . . 3
    - Gancyclovir . . . . . 1
    - Valgancyclovir . . . . . 3
- Viral hepatitis
  - Entecavir . . . . . 3
- Flu
  - Amantadine hydrochloride . . . . . 3
  - Oseltamivir . . . . . 3,4
- Human respiratory syncytial virus
  - Ribavirin . . . . . 2,3

*Antiprotozoal agents*
- Antimalarial
  - Quinine . . . . . 2,4

– Chloroquine . . . . . 1
– Doxycycline . . . . . 2
– Mefloquine . . . . . 2,3
– Proguanil hydrochloride + atovaquone . . . . . 3
• Anti-parasitic drugs against amoeba and trichomonas
– Metronidazole . . . . . 3
– Tinidazole . . . . . 3
• Leishmaniasis
– Sodium stibogluconate . . . . . 3
• Anti-pneumocystosis drugs
– Proguanil hydrochloride + atovaquone . . . . . 3
– Pentamidine isethionate . . . . . 3
*Antihelmintic drugs*
• Anti-cestode parasites drugs
– Teniacide
Niclosamide . . . . . 3


## Endocrine System


*Anti-diabetic agents*
• Oral blood-glucose-lowering drugs
– Sulfonylurea class
Glipizide . . . . . 3
– Other oral blood-glucose-lowering drugs
Pioglitazone . . . . . 3
Pioglitazone + metformin . . . . . 3
*Corticosteroids*
• Glucocorticoid steroids
– Betamethasone . . . . . 3
– Deflazacort . . . . . 3
– Dexamethasone . . . . . 3
– Hydrocortisone . . . . . 3
– Methylprednisolone . . . . . 3
– Triamcinolone . . . . . 3
*Female sex hormones*
• Estrogens and hormone replacement therapy
– Estradiol . . . . . 3
– Estradiol + progestin . . . . . 3
– Estriol . . . . . 3
– Estrogens conjugated + progestin . . . . . 3
– Ethinylestradiol . . . . . 3
– Tibolone . . . . . 3
• Progestinics
– Dydrogesterone . . . . . 3
– Medroxyprogesterone acetate . . . . . 3
– Norethisterone . . . . . 3
– Norethisterone + estradiol . . . . . 3
– Progesterone . . . . . 3
*Hypothalamic-hypophyseal hormones*
• Hypothalamic, adenohypophyseal hormones and antiestrogens
– Antiestrogens
Clomiphene citrate . . . . . 3
– Adenohypophyseal hormones
• Growth hormone receptor antagonists
– Pegvisomant . . . . . 3
– Thyrotropin alfa . . . . . 3
• Neurohypophyseal hormones and antagonists
– Neurohypophyseal hormones
– Terlipressin . . . . . 3
*Bone metabolism regulators*
• Calcitonin and parathyroid hormone
– Salmon calcitonin . . . . . 3
– Parathyroid hormone . . . . . 3
– Teriparatide . . . . . 3
• Bisphosphonates and other bone metabolism regulators
– Bisphosphonates
Pamidronate . . . . . 3
Risedronate . . . . . 2,3
Zoledronate . . . . . 3
*Other endocrine drugs*
• Gonadotropins regulators
– Antagonists and inhibitors
Danazol . . . . . 3
Ganirelix . . . . . 3
– Gonadorelin analogue
Buserelin . . . . . 3,4
Goserelin . . . . . 3
Leuprorelin acetate . . . . . 3
Triptorelin . . . . . 3


## Obstetric, Gynecology and Urology


*Obstetric drugs*
• Prostaglandins and oxytocic drugs
– Dinoprostone . . . . . 3
– Ergometrine maleate . . . . . 2,3
– Gemeprost . . . . . 3
• Tocolytic drugs
– Atosiban . . . . . 3
*Drugs used for vaginal atrophy*
• Topical hormone replacement therapy
– Topical estrogens . . . . . 3
*Hormonal contaceptives*
• Vaginal route
– Etonogestrel + ethinylestradiol . . . . . 3
*Emergency contraception (post-coital)*
• Hormonal methods
– Levonorgestrel . . . . . 3
*Progestin contraceptives*
• Progestin contraceptives (oral route) . . . . . 3
*Drugs used for genito-urinary disorders*
• Drugs used for urinary retention
– Alpha blockers
Alfuzosin hydrochloride . . . . . 3
Doxazosin . . . . . 3
Tamsulosin hydrochloride . . . . . 3
Terazosin . . . . . 3
*Drugs used for urinary disorders and incontinence*
• Urinary incontinence
– Duloxetine . . . . . 3
– Flavoxate hydrochloride . . . . . 3
– Oxibutynin hydrochloride . . . . . 3
*Drugs used in erectile dysfunction*
• Alprostadil . . . . . 3
*Phosphodiesterase type 5 inhibitors*
• Sildenafil . . . . . 3

- Tadalafil . . . . . 3
- Vardenafil . . . . . 3

### Tumors and Immunosuppresssion

*Cytotoxic drugs*
- Vinca alkaloid and etoposide
  - Etoposide . . . . . 1
  - Vinblastine solphate . . . . . 1
  - Vincristine solphate . . . . . 1
  - Vindesine solphate . . . . . 1
  - Vinorelbine . . . . . 1

*Other antineoplastic drugs*
- Cetuximab . . . . . 3
- Platinum derivatives
  - Carboplatin . . . . . 1
  - Cisplatin . . . . . 1
  - Oxaliplatin . . . . . 1
- Protein kinase inhibitors
  - Dasatinib . . . . . 2,3
  - Imatinib . . . . . 2,3
  - Sorafenib . . . . . 2
  - Sunitinib . . . . . 3
- Trastuzumab
  - Trastuzumab . . . . . 3
- Tretinoin
  - Tretinoin . . . . . 3,4

*Drugs altering immune system response*
- Drugs suppressing the immune system
  - Mefenamic acid . . . . . 3
  - Azathioprine . . . . . 3
- Corticosteroids and other immunosuppressors
  - Tacrolimus . . . . . 3,4

*Other immunomodulator drugs*
- Natalizumab
  - Natalizumab . . . . . 3

*Sex hormones and hormone antagonists in tumors*
- Progestinics
  - Medroxyprogesterone acetate . . . . . 3
  - Megestrol acetate . . . . . 3
  - Norethisterone . . . . . 3
- Hormone antagonists
  - Breast cancer
    - Exemestane . . . . . 3
    - Letrozole . . . . . 3
    - Toremifene . . . . . 3
- Prostate cancer and gonadotropin releasing hormone agonist
  - Buserelin . . . . . 3,4
  - Flutamide . . . . . 3
  - Goserelin . . . . . 3
  - Leuprorelin acetate . . . . . 3
  - Triptorelin . . . . . 3

### Blood and Nutrition

*Anemia and other hematic disorders*
- Iron deficiency anemia
  - Iron injection for anemia
    - Iron sucrose injection . . . . . 3
- Drugs used in megaloblastic anemia
  - Hydroxocobalamin . . . . . 3
- Drugs used in hypoplastic and hemolytic anemias and in anemia in kidney diseases
  - Iron-chelating agents
    - Deferoxamine mesylate . . . . . 3,4
- Drugs used for treatment of essential thrombocytosis
  - Anagrelide . . . . . 3

*Minerals*
- Hypercalcaemia and hypercalciuric
  - Cinacalcet . . . . . 3

*Vitamins*
- Vitamins d
  - Alfacalcidol . . . . . 3
  - Calcitriol . . . . . 3
  - Cholecalciferol . . . . . 3
  - Dihydrotachysterol . . . . . 3
  - Ergocalciferol . . . . . 3
  - Paricalcitol . . . . . 3

*Metabolic disorders*
- Drugs used in metabolic disorders
  - Fabry disease
    - Agalsidase alfa - beta . . . . . 2,3
  - Gaucher disease
    - Imiglucerase . . . . . 3
    - Miglustat . . . . . 3

### Muscle Skeletal System

*Drugs used in rheumatological diseases and gout*
- Non steroidal anti inflammatory drugs
  - Aceclofenac . . . . . 2,3
  - Mefenamic acid . . . . . 2,3
  - Tiaprofenic acid . . . . . 2,3
  - Acetylsalicilic acid . . . . . 1
  - Celecoxib . . . . . 2,3
  - Dexibuprofene . . . . . 2,3
  - Dexketoprofene . . . . . 2,3
  - Diclofenac potassium . . . . . 2,3
  - Diclofenac sodium . . . . . 2,3
  - Diclofenac + misoprostol . . . . . 2,3
  - Etoricoxib . . . . . 2,3
  - Flurbiprofen . . . . . 2,3
  - Ibuprofen . . . . . 2,3
  - Indomethacin . . . . . 2,3
  - Ketoprofen . . . . . 2,3
  - Meloxicam . . . . . 2,3
  - Nabumetone . . . . . 2,3
  - Naproxen . . . . . 2,3
  - Piroxicam . . . . . 2,3
  - Sulindac . . . . . 2,3
  - Tenoxicam . . . . . 2,3
- Drugs modifying the rheumatic diseases course
  - Antimalarial drugs
    - Chloroquine . . . . . 1
    - Hydroxichloroquine sulphate . . . . . 1
  - Drugs modifying the immune response

Azathioprine . . . . . 3
Leflunomide . . . . . 3
Metotrexate . . . . . 3
– Cytokines inhibitors
Adalimumab . . . . . 3
Infliximab . . . . . 3
Sulfasalazine . . . . . 2,3
• Gout and hyperuricemia cytotoxic drugs induced
– Gout long-term control
Allopurinol . . . . . 3
*Drugs used in neuromuscolar diseases*
• Skeletal muscle relaxants
– Baclofen . . . . . 3
– Dantrolene sodium . . . . . 3
– Diazepam . . . . . 3
– Tizanidine . . . . . 3
• Limbs night cramps
Quinine . . . . . 2,4


## Eye Medicaments


*Antinfective eye preparations*
• Antibacterial
– Ciprofloxacin . . . . . 2,3,4
– Gentamycin . . . . . 1
– Levofloxacin . . . . . 3,4
– Neomycin + antibiotics . . . . . 1
– Neomycin + corticosteroid . . . . . 1
– Ofloxacin . . . . . 3
– Tobramycin . . . . . 1
*Corticosteroids and other anti inflammatory preparations*
• Corticosteroids and associated antibacterials
– Dexamethasone + neomycin . . . . . 1
– Dexamethasone + netilmycin . . . . . 1
– Dexamethasone + tobramycin . . . . . 1
– Fluocinolone acetonide + neomycin . . . . . 1
– Fluorometholone + gentamycin . . . . . 1
– Hydrocortisone + neomycin + cloramfenicol . . 1
– Prednisolone + neomycin . . . . . 1
• Other anti inflammatory preparations
– Lodoxamide . . . . . 3
– Olopatadine . . . . . 3
*Mydriatic and cycloplegics*
• Antimuscarinics
– Atropine solphate . . . . . 3
– Cyclopentolate hydrochloride . . . . . 3
– Homatropine bromhydrate . . . . . 3
– Tropicamide . . . . . 3
*Glaucoma treatment*
• Beta blockers
– Timolol maleate . . . . . 2,3
• Sympathomimetics
– Brimonidine tartrate . . . . . 3
– Brimonidine tartrate + timolol . . . . . 3
• Carbonic anhydrase inhibitors and systemic drugs
– Acetazolamide . . . . . 3,4
– Brinzolamide . . . . . 3
– Dorzolamide . . . . . 3
– Dorzolamide + timolol . . . . . 3
*Diagnostic and perioperative preparations, photodynamic treatment*
• Perioperative ocular drugs
– Aproclonidin . . . . . 3
– Diclofenac sodium . . . . . 2,3
– Flurbiprofen sodium . . . . . 2,3
• Retrofoveal choroid neovascularization
– Pegaptanib sodium . . . . . 1


## Ear, Nose and Oropharynx


*Anti-inflammatory steroids and associated antimicrobial*
• Ciprofloxacin + hydrocortisone . . . . . 2,3,4
• Neomycin + fluocinolone acetonide . . . . . 1
• Polymyxin b sulphate + neomycin sulphate +
• Lidocaine hydrochloride . . . . . 1
• Polimyxyn b sulphate + neomycin sulphate +
• Lidocaine hydrochloride + hydrocortisone . . . . . 1
• Tobramycin . . . . . 1
• Tobramycin + dexamethasone . . . . . 1
*Drugs used for oropharynx*
• Drugs used for oral ulceration and inflammation
– Flurbiprofen . . . . . 2,3
• Treatment of oral dryness
– Systemic treatment
Pilocarpine hydrochloride . . . . . 3


## Skin


*Eczema and psoriasis preparations*
• Immune response regulators
– Azathioprine . . . . . 3
– Infliximab . . . . . 3
– Metotrexate . . . . . 3
*Acne and rosacea*
• Topical anti acne preparations
– Topical retinoids and anti acne preparations
Tretinoin . . . . . 3,4
• Anti acne preparations (oral route)
– Oral anti acne antibiotics
Doxycycline . . . . . 2
Erythromycin (reversible hearing loss at high dosages) . . . . . 4
Minocycline . . . . . 1
– Oral retinoid used for acne
Isotretinoin . . . . . 4
*Protective substances against uv radiations*
• Photodamage
– Diclofenac sodium . . . . . 2,3
*Anti infective skin preparations*
• Anti bacterial preparations
– Topical anti bacterial preparations (if you have to treat a large area of skin ototoxicity may be a risk associated with aminoglycosides and polymyxin use)
Neomycin sulphate . . . . . 1
Polymyxin . . . . . 1
• Anti mycotic preparations
– Ketoconazole . . . . . 3

### Immunological Medicines and Vaccines

*Cholera vaccine* . . . . . 3
*Meningococcal vaccine*
*Meningococcal group c polysaccharide*
• Conjugate vaccine . . . . . 3
• Meningococcal acwy vaccine . . . . . 3

### Anesthesia

*General anesthesia*
• Intravenous anesthetics
  – Propofol . . . . . 3
• Antimuscarinic drugs
  – Atropine . . . . . 3
  – Scopolamine hydrobromide . . . . . 3
• Perioperative analgesic and sedative drugs
  – Anxiolytics and neuroleptics
    Diazepam . . . . . 3
    Lorazepam . . . . . 3
    Midazolam . . . . . 3
    Temazepam . . . . . 3
  – Opioids analgesics
    Alfentanil . . . . . 3
    Fentanyl . . . . . 3
    Remifentanil . . . . . 3
• Drugs used in malignant hyperthermia
  – Dantrolene sodium . . . . . 3
*Local anesthesia*
• Lidocaine
  – Lidocaine hydrochloride . . . . . 3

## Sub-index A1

### Ototoxic Drugs

(Ototoxicity may include both the possible associated symptomatology of labyrinthical alteration vertigo and the possible generation of tinnitus).

### Cardiovascular System

*Diuretics*
• Loop diuretics
  – Furosemide
  – Torsemide (usually in high and rapid parenteral administration and in renal failure)

### Central Nervous System

*Analgesics*
• Non opioid analgesic
  – Acetylsalicylic acid
• Anti migraine drugs
  – Migraine acute treatment
    Acetylsalicylic acid

### Infectious Diseases

*Antibiotics*
• Other beta lactamase antibiotics
  – Imipenem + cilastatin
• Tetracyclines
  – Minocycline
• Aminoglycosides
  – Amikacin
  – Gentamycin
  – Netilmycin
  – Tobramycin
• Macrolides
  – Azithromycin
  – Clarithromycin
  – Erythromycin
• Other antibiotics
  – Teicoplanin
  – Vancomycin
• Antituberculosis drugs
  – Streptomycin
• Antifungal drugs
  – Amphotericin b
*Antiviral drugs*
• Herpes virus infection
  – Citomegalovirus
    Ganciclovir
*Antiprotozoal agents*
• Antimalarial
  – Chloroquine

### Tumors and Immunosuppresssion

*Cytotoxic drugs*
• Vinca alkaloid and etoposide
  – Etoposide
  – Vinblastine solphate
  – Vincristine solphate
  – Vindesine solphate
  – Vinorelbine
*Other antineoplastic drugs*
• Platinum derivatives
  – Carboplatin
  – Cisplatin
  – Oxaliplatin

### Muscle Skeletal System

*Drugs used for rheumatological diseases and gout*
• Non steroidal anti inflammatory drugs
  – Acetylsalicilic acid
• Drugs that modify the rheumatic diseases course
  – Antimalarial drugs
    Chloroquine
    Hydroxichloroquine sulphate

### Eye Medicaments

*Antinfective eye preparations*

- Antibacterial
  - Gentamycin
  - Neomycin + antibiotics
  - Neomycin + corticosteroid
  - Tobramycin

*Corticosteroids and other anti inflammatory preparations*
- Corticosteroids and associated antibacterials
  - Dexamethasone + neomycin
  - Dexamethasone + netilmycin
  - Dexamethasone + tobramycin
  - Fluocinolone acetonide + neomycin
  - Fluorometholone + gentamycin
  - Hydrocortisone + neomycin + cloramfenicol
  - Prednisolone + neomycin

*Diagnostic and perioperative preparations, photodynamic treatment*
- Retrofoveal choroid neovascularization
  - Pegaptanib sodium

### Ear, Nose and Oropharynx

*Anti-inflammatory steroids and associated antimicrobial*
- Neomycin + fluocinolone acetonide
- Polymyxin b sulphate + neomycin sulphate + lidocaine hydrochloride
- Polimyxyn b sulphate + neomycin sulphate + lidocaine hydrochloride + hydrocortisone
- Tobramycin
- Tobramycin + dexamethasone

### Skin

*Acne and rosacea*
- Anti acne preparations (oral route)
  - Oral anti acne antibiotics
    - Erythromycin
    - Minocycline

*Anti infective skin preparations*
- Anti bacterial preparations
  - Topical anti bacterial preparations (if you have to treat a large area of skin ototoxicity may be a risk associated with aminoglycosides and polymyxin use)
    - Neomycin sulphate
    - Polymyxin

## Sub-index A2

### Drugs Tinnitus-Generating

(There is no mention of ototoxicity).

### Gastrointestinal System

*Chronic intestinal disorders*
- Aminosalicylates
  - Sulfasalazine

### Cardiovascular System

*Diuretics*
- Potassium-sparing and other diuretics
  - Amiloride and hydrochlorothiazide

*Anti-arrhythmics*
- Supraventricular and ventricular arrhythmias
  - Flecainide acetate

*Beta blockers*
- Timolol maleate

*Hypertension and heart failure*
- Drugs used for regulate renin-angiotensin system
  - Ace inhibitors
    - Enalapril maleate
    - Enalapril+diuretics
    - Moexipril hydrochloride
    - Moexipril+diuretics
  - Angiotensin ii receptor blockers
    - Irbesartan
    - Irbesartan+diuretics
    - Valsartan + diuretics
- Nitrates, calcium channel blockers and other drugs used for angina
  - Calcium channel blockers
    - Amlodipine
    - Nicardipine hydrochloride

*Lipid – lowering medications*
- Statins
  - Atorvastatin

### Respiratory System

*Antihistamines and drugs used for alleric reactions*
- Sedative antihistamines
  - Chlorpheniramine maleate

### Central Nervous System

*Antidepressants*
- Tricyclic antidepressants and related drugs
  - Tricyclic antidepressant
    - Amitriptyline hydrochloride
    - Amitriptyline hydrochloride + perphenazine
    - Clomipramine hydrochloride
    - Dosulepin hydrochloride
    - Fluphenazine/ nortriptyline
    - Imipramine hydrochloride
    - Nortriptyline
    - Trimipramine
  - Related antidepressant
    - Mianserin hydrochloride
    - Trazodone hydrochloride
- Selective serotonin reuptake inhibitors
  - Citalopram
- Other antidepressants
  - Venlafaxine

*Drugs used in nausea and vertigo*
- Serotonin antagonists (5-ht3 receptor antagonists)
  - Palonosetron

- Neurokinin receptor antagonists
  - Aprepitant

*Analgesics*
- Opioid analgesics
  - Buprenorphine
- Anti migraine drugs
  - Migraine acute treatment
    NSAIDs
  - 5-hydroxy tryptamine agonists
    Almotriptan
    Eletriptan
    Frovatriptan

*Antiepileptic drugs*
- Epilepsy control
  - Gabapentin

*Drugs addiction*
- Cigarette smoke
  - Bupropion
  - Nicotine drug facts
  - Varenicicline
- Opioid dependence
  - Buprenorphine

*Drugs used for dementia*
- Galantamine

### Infectious Diseases

*Antibiotics*
- Tetracycline
  - Doxycycline
- Other antibiotics
  - Linezolid
- Sulfonamides and trimethoprim
  - Sulfadiazine
  - Sulfamethoxazole+trimethoprim
- Fluoroquinolones
  - Ciprofloxacin
  - Norfloxacin

*Antifungal drugs*
- Voriconazole

*Antiviral drugs*
- Human respiratory syncytial virus
  - Ribavirin

*Antiprotozoal agents*
- Antimalarial
  - Doxycycline
  - Mefloquine
  - Quinine

### Endocrine System

*Bone metabolism regulators*
- Bisphosphonates and other bone metabolism regulators
  - Bisphosphonates
    Risedronate

### Obstetric, Gynecology and Urology

*Obstetric drugs*
- Prostaglandins and oxytocic drugs
  - Ergometrine maleate

### Tumors and Immunosuppresssion

*Other antineoplastic drugs*
- Protein kinase inhibitors
  - Dasatinib
  - Imatinib
  - Sorafenib

### Blood and Nutrition

*Metabolic disorders*
- Drugs used in metabolic disorders
  - Fabry disease
    Agalsidase alfa-beta

### Muscle Skeletal System

*Drugs used in rheumatological diseases and gout*
- Non steroidal anti inflammatory drugs
  - Aceclofenac
  - Celecoxib
  - Dexibuprofene
  - Dexketoprofene
  - Diclofenac potassium
  - Diclofenac sodium
  - Diclofenac + misoprostol
  - Etoricoxib
  - Flurbiprofen
  - Ibuprofen
  - Indomethacin
  - Ketoprofen
  - Mefenamic acid
  - Meloxicam
  - Nabumetone
  - Naproxen
  - Piroxicam
  - Sulindac
  - Tenoxicam
  - Tiaprofenic acid
- Drugs modifying the rheumatic diseases course
  - Cytokines inhibitors
    Sulfasalazine

*Drugs used in neuromuscolar diseases*
- Skeletal muscle relaxants
  - Limbs night cramps
    Quinine

### Eye Medicaments

*Antinfective eye preparations*
- Antibacterial
  - Ciprofloxacin

*Glaucoma treatment*
- Beta blockers
  - Timolol maleate

*Diagnostic and perioperative preparations, photodynamic treatment*
- Perioperative ocular drugs
  - Diclofenac sodium
  - Flurbiprofen sodium

### Ear, Nose and Oropharynx

*Anti-inflammatory steroids and associated antimicrobial*
- Ciprofloxacin + hydrocortisone

*Drugs used for oropharynx*
- Drugs used for oral ulceration and inflammation
  - Flurbiprofen

### Skin

*Acne and rosacea*
- Anti acne preparations (oral route)
  - Oral anti acne antibiotics
    Doxycycline

*Protective substances against uv radiations*
- Photodamage
  - Diclofenac sodium

## Sub-index A3

### Drugs vertigo-generating

(There is no mention of ototoxicity).

### Gastrointestinal System

*Antispasmotic and other drugs used for intestinal motility disorders*
- Antimuscarinic
  - Butylscopolamine bromide
  - Propantheline bromide
  - Sulphate atropine

*Antisecretory and protective drugs on gastric mucosa*
- H2 blockers
  - Cimetidine
  - Famotidine
  - Nizatidine
  - Ranitidine
- Chelates and complexes
  - Sucralfate
- Prostaglandins analogues
  - Misoprostol
- Proton pump inhibitors
  - Esomeprazole
  - Lansoprazole
  - Omeprazole
  - Pantoprazole
  - Rabeprazole sodium

*Anti-diarrheal drugs*
- Gastrointestinal motility inhibitors
  - Loperamide hydrochloride

*Chronic intestinal disorders*
- Aminosalicylates
  - Sulfasalazine
- Cytokines inhibitors
  - Infliximab

### Cardiovascular System

*Positive inotropes*
- Cardiac glycoside
  - Digitoxin
  - Digoxin

*Diuretics*
- Thiazide and related diuretics
  - Chlorthalidone
  - Hydrochlorotiazide
  - Indapamide
- Potassium-sparing and other diuretics
  - Amiloride and hydrochlorothiazide

*Anti-arrhythmics*
- Supraventricular and ventricular arrhythmias
  - Amiodarone hydrochloride
  - Flecainide acetate
  - Propafenone hydrochloride
- Ventricular arrhythmias
  - Mexiletine hydrochloride

*Beta blockers*
- Acebutolol
- Atenolol
- Atenolol + calcium channel blockers
- Atenolol + diuretics
- Bisoprolol fumarate
- Bisoprolol fumarate + diuretics
- Carvedilol
- Celiprololo hydrochloride
- Esmolol hydrochloride
- Metoprolol tartrate
- Metoprolol + diuretics
- Nadolol
- Nebivolol
- Oxprenolol + diuretics
- Pindolol
- Propranolol hydrochloride
- Sotalol hydrochloride
- Timolol maleate

*Hypertension and heart failure*
- Anti-hypertensive vasodilators
  - Sildenafil
  - Sodium nitroprusside (related with rapid reduction of blood pressure)
- Centrally-acting anti-hypertensive drugs
  - Clonidine hydrochloride
  - Methyl dopa
  - Moxonidine
- Alpha blockers
  - Doxazosin
  - Terazosin
- Drugs used for regulate renin-angiotensin system

- – Ace inhibitors
  - Captopril
  - Captopril + diuretics
  - Cilazapril
  - Cilazapril + diuretics
  - Enalapril maleate
  - Enalapril + diuretics
  - Fosinopril
  - Fosinopril+diuretics
  - Lisinopril
  - Lisinopril + diuretics
  - Moexipril hydrochloride
  - Moexipril + diuretics
  - Perindopril
  - Perindopril + diuretics
  - Quinapril
  - Quinapril + diuretics
  - Ramipril
  - Ramipril+diuretics
  - Trandolapril
  - Trandolapril + calcium channel blockers
- – Angiotensin ii receptor blockers
  - Candesartan cilexetil
  - Candesartan + diuretics
  - Eprosartan
  - Irbesartan
  - Irbesartan + diuretics
  - Losartan potassium
  - Losartan potassium + diuretics
  - Olmesartan medoxomil
  - Olmesartan medoxomil + diuretics
  - Telmisartan
  - Telmisartan + diuretics
  - Valsartan + diuretics

• Nitrates, calcium channel blockers and other drugs used for angina
- – Nitrates
  - Nitroglycerin
  - Isosorbide dinitrate
  - Isosorbine mononitrate

• Calcium channel blockers
- Amlodipine
- Diltiazem hydrochloride
- Felodipine
- Isradipine
- Lacidipine
- Lercanidipine hydrochloride
- Nicardipine hydrochloride
- Nifedipine
- Nifedipine + atenolol
- Nisoldipine
- Verapamil hydrochloride

• Peripheral vasodilators and related drugs
- – Pentoxifylline

*Sympathomimetics*

• Cardiopulmonary resuscitation
- – Adrenaline

*Parenteral anticoagulants*

• Fondaparinux

*Anti-platelet agents*

• Clopidogrel bisulfate
• Dipyridamole

*Anti-fibrinolytic and hemostatic drugs*

• Tranexamic acid (in rapid intravenous injection)

*Blood derivatives*

• Human coagulation factor VIII
• Human coagulation factor IX

*Lipid – lowering medications*

• Fibrates
- – Bezafibrate
- – Fenofibrate
- – Gemfibrozil

• Statins
- – Atorvastatin
- – Pravastatin sodium
- – Rosuvastatin
- – Simvastatin
- – Simvastatin + ezetimibe

• Fish oil
- – Omega-3 acid ethyl esters

### Respiratory System

*Drugs used in asthma and chronic obstructive pulmonary disease*

• Adrenergic receptor agonists (sympathomimetics)
- – Beta 2 selective agonists
  - Salmeterol

• Antimuscarinic bronchodilators
- – Tiotropium

*Cromoglycate, related therapies and anti-leukotrienes*

• Anti-leukotrienes
- – Montelukast

*Antihistamines and drugs used for alleric reactions*

• Sedative antihistamines
- – Ketotifen

• Allergen immunotherapy
- – Omalizumab

### Central Nervous System

*Hypnotic and anxiolytic drugs*

• Hypnotics
- – Benzodiazepines
  - Diazepam
  - Flurazepam
  - Lormetazepam
  - Nitrazepam
  - Temazepam
- – Zaleplon, zolpidem e zopiclone
  - Zaleplon
  - Zolpidem tartrate
  - Zopiclone
- – Sodium oxybate
  - Sodium oxybate

• Anxiolytics

- – Benzodiazepines
  - Alprazolam
  - Chlordiazepoxide
  - Diazepam
  - Lorazepam
  - Oxazepam
- – Buspirone
  - Buspirone hydrochloride
- – Meprobamate
  - Meprobamate

*Barbiturates*

- Phenobarbital

*Drugs used for psychosis and related disorders*

- Atypical antipsychotics
  - – Amisulpride
  - – Aripiprazole
  - – Clorazepate dipotassium
  - – Olanzapine
  - – Quetiapine
  - – Risperidone

*Antidepressants*

- Tricyclic antidepressants and related drugs
  - – Tricyclic antidepressant
    - Amitriptyline hydrochloride
    - Amitriptyline hydrochloride + perphenazine
    - Clomipramine hydrochloride
    - Dosulepin hydrochloride
    - Fluphenazine/nortriptyline
    - Imipramine hydrochloride
    - Nortriptyline
    - Trimipramine
  - – Related antidepressant
    - Mianserin hydrochloride
    - Trazodone hydrochloride
- Selective serotonin reuptake inhibitors
  - – Citalopram
  - – Escitalopram
  - – Fluoxetine
  - – Fluvoxamine maleate
  - – Paroxetine
  - – Sertraline
- Other antidepressants
  - – Duloxetine
  - – Mirtazapine
  - – Reboxetine
  - – Venlafaxina

*Central nervous system stimulants and drugs used for attention deficit disorders and hyperactivity*

- Atomoxetine
- Metilphenidate hydrochloride
- Modafinil

*Drugs used in nausea and vertigo*

- Serotonin antagonists (5-ht3 receptor antagonists)
  - – Dolasetron mesylate
  - – Ondansetrone
  - – Palonosetron
  - – Tropisetron
- Neurokinin receptor antagonists
  - – Aprepitant
- Scopolamine
  - – Scopolamine hydrobromide

*Analgesics*

- Non opioid analgesic
  - – Paracetamol + codeine phosphate
- Opioid analgesics
  - – Buprenorphine
  - – Fentanyl
  - – Methadone hydrochloride
  - – Morphine
  - – Oxycodone hydrochloride
  - – Pentazocine
  - – Pethidine hydrochloride
  - – Tramadol

*Neuropathic pain (trigeminal neuralgia)*

- – Carbamazepine
- – Oxcarbazepine

*Anti migraine drugs*

- – Migraine acute treatment
  - Nsaids
- – 5-hydroxy tryptamine agonists
  - Almotriptan
  - Eletriptan
  - Frovatriptan
  - Rizatriptan
  - Sumatriptan
  - Zolmitriptan
- – Ergot alkaloids drugs
  - Ergotamine tartrate
- – Migraine prophylaxis
  - Pizotifen

*Antiepileptic drugs*

- Epilepsy control
  - – Carbamazepine
  - – Clobazam
  - – Clonazepam
  - – Ethosuximide
  - – Gabapentin
  - – Lamotrigine
  - – Levetiracetam
  - – Oxcarbazepine
  - – Phenytoin
  - – Pregabalin
  - – Primidone
  - – Tiagabine
  - – Topiramate
  - – Vigabatrin
  - – Zonisamide
- Drugs used for status epilepticus
  - – Clonazepam
  - – Diazepam
  - – Phenytoin sodium
  - – Lorazepam

*Parkinsonism and related disorders drugs*

- Dopaminergic drugs used for parkinsonism
  - – Dopamine receptor agonists
    - Cabergoline
    - Levodopa + benserazide

Levodopa + carbidopa
Levodopa + carbidopa + entacapone
Lisuride maleate
Pergolide
Pramipexole
Ropinirole
– Monoamine oxidase b inhibitors
Resagiline
Selegiline hydrochloride
– Catechol o methyltransferase inhibitors
Amantadine hydrochloride
Entacapone
– Antimuscarinic drugs used for parkinsonism
Orphenadrine hydrochloride
Trihexyphenidyl hydrochloride
– Drugs used for essential tremor, corea, tic and related disorders
Riluzole
– Torsional dystonia and other involuntary movements
Botulinum toxin A

*Drugs addiction*

• Alcohol dependence
– Benzodiazepines
• Cigarette smoke
– Bupropion
– Nicotine drug facts
– Varenicicline
• Opioid dependence
– Buprenorphine
– Methadone hydrochloride
– Naltrexone hydrochloride

*Drugs used for dementia*

• Donepezil hydrochloride
• Galantamine
• Memantine hydrochloride
• Rivastigmine

## Infectious Diseases

*Antibiotics*

• Penicillins
– Broad-spectrum penicillins
Amoxycillin + clavulanate
• Cephalosporins and other beta lactamase
– Cephalosporins and cephamycins
Cefaclor
Cefadroxil
Cefazolin sodium
Cefixime
Cefotaxime
Cefpodoxime
Cefprozil
Cefradine
Ceftazidime
Ceftriaxone
Cefuroxime
Cephalexin
• Other beta lactamase antibiotics
– Aztreonam
– Ertapenem
• Tetracycline
– Tigecicline
• Macrolides
– Telithromycin
• Other antibiotics
– Daptomycin
– Linezolid
– Quinupristin + dalfopristin
• Polymyxin antibiotics
– Colistin
• Sulfonamides and trimethoprim
– Sulfadiazine
– Sulfamethoxazole + trimethoprim
• Antituberculosis drugs
– Isoniazid
– Rifampicin
– Rifampicin + isoniazid
• Metronidazole and tinidazole
– Metronidazole
– Tinidazole
• Fluoroquinolones
– Ciprofloxacin
– Levofloxacin
– Moxifloxacin
– Norfloxacin
– Ofloxacin
• Antifungal drugs
– Fluconazole
– Flucytosine
– Griseofulvin
– Itraconazole
– Posaconazole
– Terbinafinae
– Voriconazole

*Antiviral drugs*

• Human immunodeficiency virus
– Nucleoside analog reverse transcriptase inhibitors
Abacavir
Abacavir + lamivudine
Abacavir + lamivudina+zidovudine
Didanosine
Emtricitabine
Emtricitabine + tenofovir
Lamivudinae
Stavudine
Tenofovir disoproxil
Zidovudine
Zidovudine + lamivudine
– Protease inhibitors
Atazanavir
Fosamprenavir
Indinavir
Lopinavir + ritonavir
Ritonavir
Saquinavir
Tipranavir

  - Non-nucleoside reverse transcriptase inhibitors
    Efavirenz
  - Other antiretroviral drugs
    Enfuvirtide
- Herpes virus infection
  - Herpes simplex and zoster
    Acyclovir
    Famcyclovir
    Inosine pranobex
    Valacyclovir
  - Citomegalovirus
    Foscarnet sodium
    Valgancyclovir
- Viral hepatitis
  - Entecavir
- Flu
  - Amantadine hydrochloride
  - Oseltamivir
- Human respiratory syncytial virus
  - Ribavirin

*Antiprotozoal agents*
- Antimalarial
  - Mefloquine
  - Proguanil hydrochloride + atovaquone
- Anti-parasitic drugs against amoeba and trichomonas
  - Metronidazole
  - Tinidazole
- Leishmaniasis
  - Sodium stibogluconate
- Anti-pneumocystosis drugs
  - Pentamidine isethionate
  - Proguanil hydrochloride + atovaquone

*Antihelmintic drugs*
- Anti-cestode parasites drugs
  - Teniacide
    Niclosamide

## Endocrine System

*Anti-diabetic agents*
- Oral blood-glucose-lowering drugs
  - Sulfonylurea class
    Glipizide
  - Other oral blood-glucose-lowering drugs
    Pioglitazone
    Pioglitazone + metformin

*Corticosteroids*
- Glucocorticoid steroids
  - Betamethasone
  - Deflazacort
  - Dexamethasone
  - Hydrocortisone
  - Methylprednisolone
  - Triamcinolone

*Female sex hormones*
- Estrogens and hormone replacement therapy
  - Estradiol
  - Estradiol + progestin
  - Estriol
  - Estrogens conjugated + progestin
  - Ethinylestradiol
  - Tibolone
- Progestinics
  - Dydrogesterone
  - Medroxyprogesterone acetate
  - Norethisterone
  - Norethisterone + estradiol
  - Progesterone

*Hypothalamic-hypophyseal hormones*
- Hypothalamic, adenohypophyseal hormones and antiestrogens
  - Antiestrogens
    Clomiphene citrate
  - Adenohypophyseal hormones
- Growth hormone receptor antagonists
  - Pegvisomant
  - Thyrotropin alfa
- Neurohypophyseal hormones and antagonists
  - Neurohypophyseal hormones
    Terlipressin

*Bone metabolism regulators*
- Calcitonin and parathyroid hormone
  - Parathyroid hormone
  - Salmon calcitonin
  - Teriparatide
- Bisphosphonates and other bone metabolism regulators
  - Bisphosphonates
    Pamidronate
    Risedronate
    Zoledronate

*Other endocrine drugs*
- Gonadotropins regulators
  - Antagonists and inhibitors
    Danazol
    Ganirelix
  - Gonadorelin analogue
    Buserelin
    Goserelin
    Leuprorelin acetate
    Triptorelin

## Obstetric, Gynecology and Urology

*Obstetric drugs*
- Prostaglandins and oxytocic drugs
  - Dinoprostone
  - Ergometrine maleate
  - Gemeprost
- Tocolytic drugs
  - Atosiban

*Drugs used for vaginal atrophy*
- Topical hormone replacement therapy
  - Topical estrogens

*Hormonal contraceptives*
- Vaginal route
  - Etonogestrel + ethinylestradiol

*Emergency contraception (post-coital)*
- Hormonal methods
  - Levonorgestrel

*Progestin contraceptives*
- Progestin contraceptives (oral route)

*Drugs used for genito-urinary disorders*
- Drugs used for urinary retention
  - Alpha blockers
    Alfuzosin hydrochloride
    Doxazosin
    Tamsulosin hydrochloride
    Terazosin

*Drugs used for urinary disorders and incontinence*
- Urinary incontinence
  - Duloxetine
  - Flavoxate hydrochloride
  - Oxibutynin hydrochloride

*Drugs used in erectile dysfunction*
- Alprostadil

*Phosphodiesterase type 5 inhibitors*
- Sildenafil
- Tadalafil
- Vardenafil

### Tumors and Immunosuppresssion

*Other antineoplastic drugs*
- Cetuximab
- Protein kinase inhibitors
  - Dasatinib
  - Imatinib
  - Sunitinib
- Trastuzumab
  - Trastuzumab
- Tretinoin
  - Tretinoin

*Drugs altering immune system response*
- Drugs suppressing the immune system
  - Azathioprine
  - Mefenamic acid
- Corticosteroids and other immunosuppressors
  - Tacrolimus

*Other immunomodulator drugs*
- Natalizumab
  - Natalizumab

*Sex hormones and hormone antagonists in tumors*
- Progestinics
  - Medroxyprogesterone acetate
  - Megestrol acetate
  - Norethisterone
- Hormone antagonists
  - Breast cancer
  - Exemestane
  - Letrozole
  - Toremifene
- Prostate cancer and gonadotropin releasing hormone agonist
  - Buserelin
  - Flutamide
  - Goserelin
  - Leuprorelin acetate
  - Triptorelin

### Blood and Nutrition

*Anemia and other hematic disorders*
- Iron deficiency anemia
  - Iron injection for anemia
    Iron sucrose injection
- Drugs used in megaloblastic anemia
  - Hydroxocobalamin
- Drugs used in hypoplastic and hemolytic anemias and in anemia in kidney diseases
  - Iron-chelating agents
    Deferoxamine mesylate
- Drugs used for treatment of essential thrombocytosis
  - Anagrelide

*Minerals*
- Hypercalcaemia and hypercalciuric
  - Cinacalcet

*Vitamins*
- Vitamins d
  - Alfacalcidol
  - Calcitriol
  - Cholecalciferol
  - Dihydrotachysterol
  - Ergocalciferol
  - Paricalcitol

*Metabolic disorders*
- Drugs used for metabolic disorders
  - Fabry disease
    Agalsidase alfa - beta
  - Gaucher disease
    Imiglucerasi
    Miglustat

### Muscle Skeletal System

*Drugs used in rheumatological diseases and gout*
- Non steroidal anti inflammatory drugs
  - Aceclofenac
  - Celecoxib
  - Dexibuprofene
  - Dexketoprofene
  - Diclofenac potassium
  - Diclofenac sodium
  - Diclofenac + misoprostol
  - Etoricoxib
  - Flurbiprofen
  - Ibuprofen
  - Indomethacin
  - Ketoprofen
  - Mefenamic acid
  - Meloxicam
  - Nabumetone
  - Naproxen
  - Piroxicam
  - Sulindac

  - Tenoxicam
  - Tiaprofenic acid
- Drugs modifying the immune response
  - Azathioprine
  - Leflunomide
  - Metotrexate
- Cytokines inhibitors
  - Adalimumab
  - Infliximab
  - Sulfasalazine
- Gout and hyperuricemia cytotoxic drugs induced
  - Gout long-term control
    Allopurinol

*Drugs used in neuromuscolar diseases*
- Skeletal muscle relaxants
  - Baclofen
  - Dantrolene sodium
  - Diazepam
  - Tizanidine

### Eye Medicaments

*Antinfective eye preparations*
- Antibacterial
  - Ciprofloxacin
  - Levofloxacin
  - Ofloxacin

*Corticosteroids and other anti inflammatory preparations*
- Other anti inflammatory preparations
  - Lodoxamide
  - Olopatadine

*Mydriatic and cycloplegics*
- Antimuscarinics
  - Atropine solphate
  - Cyclopentolate hydrochloride
  - Homatropine bromhydrate
  - Tropicamide

*Glaucoma treatment*
- Beta blockers
  - Timolol maleate
- Sympathomimetics
  - Brimonidine tartrate
  - Brimonidine tartrate + timolol
- Carbonic anhydrase inhibitors and systemic drugs
  - Acetazolamide
  - Brinzolamide
  - Dorzolamide
  - Dorzolamide + timolol

*Diagnostic and perioperative preparations, photodynamic treatment*
- Perioperative ocular drugs
  - Aproclonidin
  - Diclofenac sodium
  - Flurbiprofen sodium

### Ear, Nose and Oropharynx

*Anti-inflammatory steroids and associated antimicrobial*
- Ciprofloxacin + hydrocortisone

*Drugs used for oropharynx*
- Drugs used for oral ulceration and inflammation
  - Flurbiprofen
- Treatment of oral dryness
  - Systemic treatment
    Pilocarpine hydrochloride

### Skin

*Eczema and psoriasis preparations*
- Immune response regulators
  - Azathioprine
  - Infliximab
  - Metotrexate

*Acne and rosacea*
- Topical anti acne preparations
  - Topical retinoids and anti acne preparations
    Tretinoin

*Protective substances against uv radiations*
- Photodamage
  - Diclofenac sodium

*Anti infective skin preparations*
- Anti mycotic preparations
  - Ketoconazole

### Immunological Medicines and Vaccines

*Cholera vaccine*
*Meningococcal vaccine*
- Meningococcal group c polysaccharide conjugate vaccine
- Meningococcal acwy vaccine

### Anesthesia

*General anesthesia*
- Intravenous anesthetics
  - Propofol
- Antimuscarinic drugs
  - Atropine
  - Scopolamine hydrobromide
- Perioperative analgesic and sedative drugs
  - Anxiolytics and neuroleptics
    Diazepam
    Lorazepam
    Midazolam
    Temazepam
  - Opioids analgesics
    Alfentanil
    Fentanyl
    Remifentanil
- Drugs used in malignant hyperthermia
  - Dantrolene sodium

*Local anesthesia*
- Lidocaine
  - Lidocaine hydrochloride

## Sub-Index A4

Drugs with possible audiologic effects, indicated as "hearing disturbances" (drugs with aspecific otologic side effects), it is advisable to have a conservative approach to these drugs and to evaluate in each case the possible intensity and type of adverse reaction.

### Central Nervous System

*Hypnotic and anxiolytic drugs*
- Hypnotics
  - Zaleplon, zolpidem e zopiclone
    Zaleplon
    Zolpidem tartrate

*Antiepileptic drugs*
- Epilepsy control
  - Pregabalin (hyperacusia)

### Infectious Diseases

*Antibiotics*
- Fluoroquinolones
  - Ciprofloxacin
  - Levofloxacin
  - Moxifloxacin
  - Norfloxacin
  - Ofloxacin

*Antifungal drugs*
  - Posaconazole
  - Voriconazole

*Antiviral drugs*
- Flu
  - Oseltamivir

*Antiprotozoal agents*
- Antimalarial
  - Quinine

### Endocrine System

*Other endocrine drugs*
- Gonadotropins regulators
  - Gonadorelin analogue
    Buserelin

### Tumors and Immunosuppresssion

*Other antineoplastic drugs*
- Tretinoin
  - Tretinoin

*Drugs altering immune system response*
- Corticosteroids and other immunosuppressors
  - Tacrolimus

*Sex hormones and hormone antagonists in tumors*
- Hormone antagonists
  - Prostate cancer and gonadotropin releasing hormone agonist
    Buserelin

### Blood and Nutrition

*Anemia and other hematic disorders*
- Drugs used in hypoplastic and hemolytic anemias and in anemia in kidney diseases
  - Iron-chelating agents
    Deferoxamine mesylate

### Muscle Skeletal System

*Drugs used in neuromuscolar diseases*
- Skeletal muscle relaxants
  - Limbs night cramps
    Quinine

### Eye Medicaments

*Antinfective eye preparations*
- Antibacterial
  - Ciprofloxacin
  - Levofloxacin

*Glaucoma treatment*
- Carbonic anhydrase inhibitors and systemic drugs
  - Acetazolamide

### Ear, Nose and Oropharynx

*Anti-inflammatory steroids and associated antimicrobial*
- Ciprofloxacin + hydrocortisone

### Skin

*Acne and rosacea*
- Topical anti acne preparations
  - Topical retinoids and anti acne preparations
    Tretinoin

*Anti acne preparations (oral route)*
- Oral retinoid used for acne
- Isotretinoin

## Index B

In this index the active principles are listed in alphabetical order, each with a numerical reference to the relevant type of side effect. Whenever possible according to data available to us, believing it to be very useful, we indicated the side effect frequency for each drug using a grading scale from a to e going from "very common" to "very rare" (see page 609).

| Reference numbers | Drugs classes | ADR | Reference numbers | Drugs classes | ADR |
|---|---|---|---|---|---|
| 1 | Abacavir + Lamivudine | 3 | 52 | Aztreonam | 3 |
| 2 | Abacavir | 3 | 53 | Bacitracin + Neomycin | 1 |
| 3 | Abacvir + Lamivudine + Zidovudine | 3 | 54 | Baclofen | 3 |
| 4 | Acebutolol | 3b | 55 | Benazepril + Hydrochlorothiazide | 2c,3b |
| 5 | Aceclidine + Timolol Maleate | 2,3 | 56 | Benazepril Hydrochloride | 2,3 |
| 6 | Aceclofenac | 2e,3e | 57 | Betamethasone + Bekanamicin + Tetryzoline | 1 |
| 7 | Acetazolamide | 3,4 | | | |
| 8 | Acetylsalicylic Acid | 1 | 58 | Betamethasone + Tetryzoline | 3 |
| 9 | Acetylsalicylic Acid + Magnesium | 1 | 59 | Betamethasone | 3 |
| 10 | Acyclovir | 3 | 60 | Betamethasone + Clorfenamin | 2,3 |
| 11 | Adalimumab | 3b | 61 | Bezafibrate | 3 |
| 12 | Adrenaline | 3 | 62 | Biperiden Hydrochloride | 3 |
| 13 | Agalsidase Alfa - Beta | 2,3 | 63 | Bisoprolol Fumarate + Diuretics | 3c |
| 14 | Alfacalcidol | 3 | 64 | Bisoprolol Fumarate | 3b |
| 15 | Alfentanil | 3 | 65 | Botulinum Toxin A | 3b |
| 16 | Alfuzosin Hydrochloride | 3 | 66 | Brimonidine Tartrate + Timolol | 3c |
| 17 | Alizapride Hydrochloride | 3 | 67 | Brimonidine Tartrate | 3b |
| 18 | Allopurinol | 3 | 68 | Brinzolamide | 3c |
| 19 | Almotriptan | 2c,3b | 69 | Bromazepam | 3 |
| 20 | Alpha 1 Antitrypsin | 3 | 70 | Bromocriptine Mesylate | 3 |
| 21 | Alprazolam | 3b | 71 | Bromperidol | 3 |
| 22 | Alprostadil | 3 | 72 | Brotizolam | 3 |
| 23 | Amantadine Hydrochloride | 3 | 73 | Buflomedil Hydrochloride | 3e |
| 24 | Ambroxol Hydrochloride | 3 | 74 | Bupivacaine + Adrenaline | 3 |
| 25 | Amifostine | 3 | 75 | Bupivacaine Hydrochloride | 3 |
| 26 | Amikacin | 1 | 76 | Buprenorphine | 2d,3b |
| 27 | Amikacin Sulphate | 1 | 77 | Bupropion | 2c,3b |
| 28 | Amiloride And Hydrochlorothiazide | 2,3 | 78 | Buserelin | 3,4 |
| 29 | Amiodarone Hydrochloride | 3 | 79 | Buspirone Hydrochloride | 3b |
| 30 | Amisulpride | 3 | 80 | Butizide + Canrenoate Potassium | 3e |
| 31 | Amitriptyline Chlordiazepoxide | 2,3 | 81 | Butylscopolamine Bromide | 3 |
| 32 | Amitriptyline Hydrochloride | 2,3 | 82 | Buxamine | 3 |
| 33 | Amitriptyline Hydrochloride + Perphenazine | 2,3 | 83 | Buxamine + Fenobarbital + Fenitoine | 3 |
| | | | 84 | Buxamine + Diazepam | 3 |
| 34 | Amlodipine | 2,3 | 85 | Cabergoline | 3b |
| 35 | Amoxycillin + Clavulanate | 3 | 86 | Cadralazine | 3 |
| 36 | Amphotericin B | 1 | 87 | Calcitriol | 3 |
| 37 | Anagrelide | 3b | 88 | Calcium Carbonate + Cholecalciferol (Vitamin D3) | 3 |
| 38 | Aniracetam | 3d | | | |
| 39 | Aprepitant | 2,3 | 89 | Calcium Channel Blockers | 3 |
| 40 | Aproclonidin | 3c | 90 | Candesartan + Diuretics | 3 |
| 41 | Aripiprazole | 3b | 91 | Candesartan Cilexetil | 3 |
| 42 | Articaine + Adrenaline | 2,3 | 92 | Captopril + Diuretics | 3 |
| 43 | Atazanavir | 3c | 93 | Captopril | 3 |
| 44 | Atenolol + Diuretics | 3 | 94 | Carbamazepine | 3a |
| 45 | Atenolol | 3 | 95 | Carboplatin | 1 |
| 46 | Atomoxetine | 3 | 96 | Carvedilol | 3a |
| 47 | Atorvastatin | 2,3 | 97 | Cefaclor | 3d |
| 48 | Atosiban | 3b | 98 | Cefadroxil | 3 |
| 49 | Atropine Sulphate | 3 | 99 | Cefazolin Sodium | 3 |
| 50 | Azathioprine | 3 | 100 | Cefepime | 2d,3d |
| 51 | Azithromycin | 1,3d | 101 | Cefixime | 3 |

| | | |
|---|---|---|
| 102 | Cefonicid Disodium | 3 |
| 103 | Cefoperazone Sodium | 3d |
| 104 | Cefotaxime | 3 |
| 105 | Cefpodoxime | 3 |
| 106 | Cefprozil | 3c |
| 107 | Ceftazidime | 3c |
| 108 | Ceftibutene | 2,3d |
| 109 | Ceftizoxime Sodium | 3 |
| 110 | Ceftriaxone | 3d |
| 111 | Cefuroxime | 3 |
| 112 | Celecoxib | 2c,3c |
| 113 | Celiprololo Hydrochloride | 3 |
| 114 | Cephalexin | 3 |
| 115 | Cephradin | 3 |
| 116 | Cetuximab | 3a |
| 117 | Chlordiazepoxide | 3 |
| 118 | Chloroquine | 1 |
| 119 | Chlorpheniramine Maleate | 2b |
| 120 | Chlorthalidone | 3 |
| 121 | Cholecalciferol | 3 |
| 122 | Chondroitin Sulphate | 3 |
| 123 | Cilazapril + Diuretics | 3 |
| 124 | Cilazapril | 3b |
| 125 | Cimetidine | 3 |
| 126 | Cimetropium Bromide | 3 |
| 127 | Cinacalcet | 3b |
| 128 | Cinoxacin | 1,2c,3b |
| 129 | Ciprofloxacin + Hydrocortisone | 2b,3c, 4d |
| 130 | Ciprofloxacin | 2d,3c, 4d |
| 131 | Cisplatin | 1a |
| 132 | Citalopram | 2b,3b |
| 133 | Clarithromicin | 1e,2d, 3e |
| 134 | Clidinium Bromide + Chlordiazepoxide | 3 |
| 135 | Clobazam | 3 |
| 136 | Clomiphene Citrate | 3c |
| 137 | Clomipramine Hydrochloride | 2b,3a |
| 138 | Clonazepam | 3 |
| 139 | Clonidine Hydrochloride | 3 |
| 140 | Clopidogrel Bisulfate | 3d |
| 141 | Clorazepate Dipotassium | 3 |
| 142 | Clotiazepam | 3 |
| 143 | Cocarboxyilase + Pyridoxine + Hydroxocobalamin | 3 |
| 144 | Codeine + Pheniramine | 3 |
| 145 | Codeine Phosphate + Ivy | 3e |
| 146 | Colistin | 3 |
| 147 | Cyclobenzaprine Hydrochloride | 2,3 |
| 148 | Cyclopentolate Hydrochloride | 3 |
| 149 | Cyproterone + Ethinyl Estradiol | 3d |
| 150 | Danazol | 3e |
| 151 | Dantrolene Sodium | 3b |
| 152 | Daptomycin | 3c |
| 153 | Dasatinib | 2c,3d |
| 154 | Deferoxamine Mesylate | 3,4 |
| 155 | Defibrotide | 3 |
| 156 | Deflazacort | 3 |
| 157 | Delapril | 3d |
| 158 | Delapril + Indapamide | 3d |
| 159 | Delorazepam | 3 |
| 160 | Desipramine Hydrochloride | 2b,3b |
| 161 | Dexamethasone | 3 |
| 162 | Dexamethasone + Neomycin | 1 |
| 163 | Dexamethasone + Netilmicin | 1 |
| 164 | Dexamethasone + Tobramycin | 1 |
| 165 | Dexibuprofene | 2c,3b |
| 166 | Dexketoprofene | 2e,3c |
| 167 | Diazepam | 3 |
| 168 | Diclofenac + Misoprostol | 2,3 |
| 169 | Diclofenac Epolamine | 2e,3e |
| 170 | Diclofenac Potassium | 2e,3e |
| 171 | Diclofenac Sodium | 2e,3e |
| 172 | Diclofenamide (Sodium) | 2,3 |
| 173 | Didanosine | 3 |
| 174 | Digitoxin | 3 |
| 175 | Digoxin | 3 |
| 176 | Dihydrocodeine | 3e |
| 177 | Dihydrocodeine + Benzoic Acid | 3e |
| 178 | Dihydrocodeine + Pentetrazol | 3e |
| 179 | Dihydroergokryptine Mesylate | 3 |
| 180 | Dihydroergotamine Mesylate | 3 |
| 181 | Dihydroquinidine Hydrochloride | 1 |
| 182 | Dihydrotachysterol | 3 |
| 183 | Diltiazem Hydrochloride | 3 |
| 184 | Dinoprostone | 3 |
| 185 | Diosmin | 3 |
| 186 | Diosmin + Hesperidin | 3 |
| 187 | Diphtheria, Tetanus Vaccine Adsorbed | 3d |
| 188 | Dipyridamole | 3e |
| 189 | Dolasetron Mesylate | 3 |
| 190 | Donepezil Hydrochloride | 3b |
| 191 | Dorzolamide | 3 |
| 192 | Dorzolamide + Timolol | 3c |
| 193 | Dosulepin Hydrochloride | 2b,3b |
| 194 | Doxazosin | 3b |
| 195 | Doxycycline | 2 |
| 196 | Duloxetine | 3c |
| 197 | Dydrogesterone | 3 |
| 198 | Efavirenz | 3c |
| 199 | Eletriptan | 2c,3b |
| 200 | Emtricitabine + Tenofovir | 3a |
| 201 | Emtricitabine | 3b |
| 202 | Enalapril + Diuretics | 2c,3c |
| 203 | Enalapril Maleate | 2c,3c |
| 204 | Enfuvirtide | 3b |
| 205 | Entacapone | 3b |
| 206 | Entecavir | 3b |
| 207 | Eprosartan | 3d |
| 208 | Ergocalciferol | 3 |
| 209 | Ergometrine Maleate | 2,3 |
| 210 | Ergotamine Tartrate | 3 |
| 211 | Ertapenem | 3 |
| 212 | Erythromycin | 1 |
| 213 | Escitalopram | 3b |
| 214 | Esmolol Hydrochloride | 3 |
| 215 | Esomeprazole | 3c |
| 216 | Estazolam | 3 |
| 217 | Estradiol + Progestin | 3c |
| 218 | Estradiol | 3c |
| 219 | Estriol | 3 |
| 220 | Estrogens Conjugated + Progestin | 3 |
| 221 | Ethacrynic Acid | 1 |
| 222 | Ethinylestradiol | 3c |
| 223 | Ethosuximide | 3 |
| 224 | Etizolam | 3 |

| | | |
|---|---|---|
| 225 | Etonogestrel + Ethinylestradiol | 3c |
| 226 | Etoposide | 1 |
| 227 | Etoricoxib | 2c,3c |
| 228 | Exemestane | 3b |
| 229 | Famciclovir | 3d |
| 230 | Famotidine | 3b |
| 231 | Felbamate | 3c |
| 232 | Felodipine | 3c |
| 233 | Fenofibrate | 3 |
| 234 | Fentanyl Citrate | 3 |
| 235 | Flavoxate Hydrochloride + Propyphenazone | 3 |
| 236 | Flavoxate Hydrochloride | 3d |
| 237 | Flecainide Acetate | 2b,3b |
| 238 | Fluconazole | 3b |
| 239 | Flucytosine | 3 |
| 240 | Fluocinolone Acetonide + Neomycin | 1 |
| 241 | Fluorometholone + Gentamycin | 1 |
| 242 | Fluoxetine | 3b |
| 243 | Fluphenazine/Nortriptyline | 2,3 |
| 244 | Flurazepam | 3 |
| 245 | Flurbiprofen Sodium | 2,3 |
| 246 | Flurbiprofen | 2,3 |
| 247 | Flurithromycin Ethylsuccinate | 3 |
| 248 | Flutamide | 3d |
| 249 | Fluvoxamine Maleate | 3b |
| 250 | Fondaparinux | 3d |
| 251 | Fosamprenavir | 3b |
| 252 | Foscarnet Sodium | 3 |
| 253 | Fosinopril | 3c |
| 254 | Fosinopril + Diuretics | 3 |
| 255 | Frovatriptan | 2c,3c |
| 256 | Furosemide | 1d,2d |
| 257 | Gabapentin | 2,3 |
| 258 | Galantamine | 2,3b |
| 259 | Gancyclovir | 1,3b |
| 260 | Ganirelix | 3 |
| 261 | Gemeprost | 3e |
| 262 | Gemfibrozil | 3e |
| 263 | Gentamycin | 1 |
| 264 | Glipizide | 3 |
| 265 | Goserelin | 3 |
| 266 | Griseofulvin | 3d |
| 267 | Haemophilus B (Meningococcal Protein Conjugate) Hepatitis B Vaccine Recombinant | 3d |
| 268 | Halcinonide + Salicylic Acid | 1 |
| 269 | Hepatitis A Inactivated & Hepatitis B (Recombinant) Vaccine | 3d |
| 270 | Hepatitis B Vaccine (Rdna) | 3d |
| 271 | Homatropine Bromhydrate | 3 |
| 272 | Human Coagulation Factor IX | 3c |
| 273 | Human Coagulation Factor VIII | 3 |
| 274 | Human Cytomegalovirus Immunoglobulin For Intravenous Administration | 3 |
| 275 | Hydrochlorotiazide | 3 |
| 276 | Hydrochlorotiazide + Spironolactone | 3 |
| 277 | Hydrocortisone | 3 |
| 278 | Hydrocortisone + Neomycin + Cloramfenicol | 1 |
| 279 | Hydroxichloroquine Sulphate | 1 |
| 280 | Hydroxocobalamin | 3 |
| 281 | Hydroxyprogesterone Caproate | 3 |
| 282 | Ibuprofen | 2d,3d |
| 283 | Icodextrin + Sodium Chloride + Sodium Lactate + Calcium Chloride + Magnesium Chloride | 3b |
| 284 | Idebenone | 3 |
| 285 | Idroxine Hydrochloride | 2,3 |
| 286 | Imatinib | 2c,3c |
| 287 | Imiglucerase | 3c |
| 288 | Imipenem + Cilastatin | 1 |
| 289 | Imipramine Hydrochloride | 2,3 |
| 290 | Indapamide | 3 |
| 291 | Indinavir | 3a |
| 292 | Indomethacin | 2,3 |
| 293 | Indomethacin + Caffeine + Proclorperazina | 2,3,4 |
| 294 | Infliximab | 3b |
| 295 | Inosine Pranobex | 3 |
| 296 | Irbesartan + Diuretics | 2e,3e |
| 297 | Irbesartan | 2 |
| 298 | Iron Sucrose Injection | 3 |
| 299 | Isoniazid + Ethambutol + Pyridoxine | 3 |
| 300 | Isoniazid | 3 |
| 301 | Isosorbide Dinitrate | 3 |
| 302 | Isosorbide Mononitrate | 3e |
| 303 | Isotretinoin | 4e |
| 304 | Isoxsuprine Hydrochloride | 3 |
| 305 | Isradipine | 3 |
| 306 | Itraconazole | 3c |
| 307 | Ketazolam | 3 |
| 308 | Ketoconazole | 3 |
| 309 | Ketoprofen | 2,3e |
| 310 | Ketorolac Tromethamine | 3,4 |
| 311 | Ketotifen | 3 |
| 312 | Lacidipine | 3 |
| 313 | Lamivudine | 3 |
| 314 | Lamotrigine | 3 |
| 315 | Lansoprazole | 3 |
| 316 | Leflunomide | 3b |
| 317 | Lercanidipine Hydrochloride | 3b |
| 318 | Lertapenem | 3c |
| 319 | Letrozole | 3b |
| 320 | Leuprorelin Acetate | 3 |
| 321 | Levetiracetam | 3b |
| 322 | Levobupivacaine Hydrochloride | 3b |
| 323 | Levodopa + Benserazide | 3 |
| 324 | Levodopa + Carbidopa | 3c |
| 325 | Levodopa + Carbidopa + Entacapone | 3c |
| 326 | Levodropropizine | 3 |
| 327 | Levofloxacin | 3c,4e |
| 328 | Levonorgestrel | 3b |
| 329 | Levosimendan | 3b |
| 330 | Lidocaine + Adrenaline | 3 |
| 331 | Lidocaine + Cetrimonium Bromide | 3 |
| 332 | Lidocaine + Hydrocortisone | 3 |
| 333 | Lidocaine + Nor Adrenaline | 3 |
| 334 | Lidocaine Hydrochloride | 3 |
| 335 | Lincomycin Hydrochloride | 2e,3e |
| 336 | Linezolid | 2c,3c |
| 337 | Lisinopril | 3b |
| 338 | Lisinopril+ Diuretics | 3b |
| 339 | Lisuride Maleate | 3e |
| 340 | Lodoxamide | 3 |
| 341 | Lomefloxacin Hydrochloride | 1b,2b, 3b |

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|---|---|---|
| 342 | Loperamide Hydrochloride | 3e |
| 343 | Lopinavir + Ritonavir | 3d |
| 344 | Lorazepam | 3b |
| 345 | Lormetazepam | 3 |
| 346 | Losartan Potassium | 3b |
| 347 | Losartan Potassium + Diuretics | 3b |
| 348 | Lysine Acetyl Salicylate | 1b,2b, 3b |
| 349 | Manidipine Hydrochloride | 3 |
| 350 | Measles, Mumps And Rubella Virus Vaccine Live Attenuated | 1e |
| 351 | Meclofenamate Sodium | 2,3 |
| 352 | Medroxyprogesterone + Estrogens Conjugated | 3 |
| 353 | Medroxyprogesterone Acetate | 3 |
| 354 | Mefenamic Acid | 2,3 |
| 355 | Mefloquine | 2,3b |
| 356 | Megestrol Acetate | 3 |
| 357 | Meloxicam | 2c,3c |
| 358 | Memantine Hydrochloride | 3b |
| 359 | Meningococcal Acwy Vaccine | 3 |
| 360 | Meningococcal Group C Polysaccharide Conjugate Vaccine | 3e |
| 361 | Mepivacaine + Adrenaline | 2,3 |
| 362 | Mepivacaine Hydrochloride | 2,3 |
| 363 | Meprobamate | 3 |
| 364 | Metformin + Glybenclamide | 3 |
| 365 | Metformin Hydrochloride | 3b |
| 366 | Methadone Hydrochloride | 3b |
| 367 | Methyl Dopa + Hydrochlorotiazide | 3e |
| 368 | Methyl Dopa | 3 |
| 369 | Methylergometrine Maleate | 2e,3e |
| 370 | Methylpranolol + Pilocarpine Hydrochloride | 3 |
| 371 | Methylprednisolone | 3 |
| 372 | Methylprednisolone + Lidocaine | 3 |
| 373 | Metilphenidate Hydrochloride | 3 |
| 374 | Metixene Hydrochloride | 3 |
| 375 | Metoprolol + Diuretics | 3e |
| 376 | Metoprolol Tartrate | 3b |
| 377 | Metotrexate | 3 |
| 378 | Metronidazole | 3e |
| 379 | Mexiletine Hydrochloride | 3d |
| 380 | Mianserin Hydrochloride | 2,3 |
| 381 | Midazolam | 3e |
| 382 | Midodrine Hydrochloride | 3 |
| 383 | Miglustat | 3a |
| 384 | Minocycline | 1,3d |
| 385 | Mirtazapine | 3b |
| 386 | Misoprostol | 3 |
| 387 | Modafinil | 3c |
| 388 | Moexipril + Diuretics | 2d,3d |
| 389 | Moexipril Hydrochloride | 2e,3e |
| 390 | Montelukast | 3d |
| 391 | Moroctocog Alfa | 3 |
| 392 | Morphine Hydrochloride | 3 |
| 393 | Morphine Hydrochloride + Atropine Sulphate | 3 |
| 394 | Moxifloxacin | 3b,4d |
| 395 | Moxonidine | 3b |
| 396 | Muromonab - Cd3 | 1 |
| 397 | Mycophenolic Acid | 3b |
| 398 | Nabumetone | 2d,3d |
| 399 | Nadolol | 3e |
| 400 | Naltrexone Hydrochloride | 3b |
| 401 | Naproxen | 2b,3d |
| 402 | Natalizumab | 3b |
| 403 | Nebivolol | 3b |
| 404 | Neomycin + Antibiotics | 1 |
| 405 | Neomycin + Corticosteroid | 1 |
| 406 | Neomycin + Dexamethasone + Gramicidin + Tetryzoline | 1 |
| 407 | Neomycin + Dexamethasone + Phenylephrine | 1 |
| 408 | Neomycin + Fluocinolone Acetonide | 1 |
| 409 | Neomycin Sulphate | 1 |
| 410 | Neostigmine Methylsulfate | 3d |
| 411 | Netilmicin | 1e |
| 412 | Nicardipine Hydrochloride | 2,3e |
| 413 | Nicergoline | 3d |
| 414 | Niclosamide | 3 |
| 415 | Nicotine Drug Facts | 2,3b |
| 416 | Nifedipine | 3d |
| 417 | Nifedipine + Atenolol | 3 |
| 418 | Nimesulide | 3c,4e |
| 419 | Nimesulide Beta – Dex | 3e,4e |
| 420 | Nisoldipine | 3 |
| 421 | Nitrazepam | 3 |
| 422 | Nitroglycerin | 3 |
| 423 | Nizatidine | 3 |
| 424 | Nordazepam | 3 |
| 425 | Norethisterone + Estradiol | 3 |
| 426 | Norethisterone Acetate | 3 |
| 427 | Norethisterone | 3 |
| 428 | Norfloxacin | 2e,3b, 4e |
| 429 | Nortriptyline | 2,3 |
| 430 | Octatropine Methyl Bromide and Diazepam | 3d |
| 431 | Ofloxacin | 3e,4e |
| 432 | Olanzapine | 3b |
| 433 | Olmesartan Medoxomil + Diuretics | 3b |
| 434 | Olmesartan Medoxomil | 3e |
| 435 | Olopatadine | 3c |
| 436 | Omalizumab | 3c |
| 437 | Omega-3 Acid Ethyl Esters | 3 |
| 438 | Omeprazole | 3c |
| 439 | Ondansetrone | 3d |
| 440 | Oral Cholera Vaccine | 3d |
| 441 | Orphenadrine Hydrochloride | 3 |
| 442 | Oseltamivir | 3b,4b |
| 443 | Otilonio Bromide | 3 |
| 444 | Otilonio Bromide + Diazepam | 3e |
| 445 | Oxaliplatin | 1c |
| 446 | Oxaprozin | 2e,3e, 4e |
| 447 | Oxazepam | 3 |
| 448 | Oxcarbazepine | 3b |
| 449 | Oxibutynin Hydrochloride | 3 |
| 450 | Oxprenolol + Diuretics | 3 |
| 451 | Oxycodone Hydrochloride | 3c |
| 452 | Palonosetron | 2c,3b |
| 453 | Pamidronate | 3c |
| 454 | Pantoprazole | 3d |
| 455 | Paracetamol + Chlorphenamine | 2,3 |
| 456 | Paracetamol + Codeine Phosphate | 3 |
| 457 | Parathyroid Hormone | 3b |
| 458 | Paricalcitol | 3c |

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|---|---|---|
| 459 | Paromomycin Sulphate | 1e |
| 460 | Paroxetine | 3b |
| 461 | Pefloxacin Mesylate | 3 |
| 462 | Pegaptanib Sodium | 1c,3c |
| 463 | Pegvisomant | 3b |
| 464 | Pentamidine Isethionate | 3 |
| 465 | Pentazocine | 3b |
| 466 | Pentoxifylline | 3 |
| 467 | Pergolide | 3a |
| 468 | Perindopril | 3b |
| 469 | Perindopril + Diuretics | 3c |
| 470 | Pethidine Hydrochloride | 3 |
| 471 | Phenobarbital | 3 |
| 472 | Phenytoin | 3 |
| 473 | Phenytoin Sodium | 3e |
| 474 | Pilocarpine Hydrochloride | 3b |
| 475 | Pindolol | 3b |
| 476 | Pioglitazone + Metformin | 3 |
| 477 | Pioglitazone | 3b |
| 478 | Pipemidic Acid | 3 |
| 479 | Piperazine | 3 |
| 480 | Piretanide | 3 |
| 481 | Piroxicam | 2d,3d |
| 482 | Pizotifen | 3 |
| 483 | Polimyxyn B Sulphate + Neomycin Sulphate + Lidocaine Hydrochloride + Hydrocortisone | 1 |
| 484 | Polymyxin B Sulphate + Neomycin Sulphate + Lidocaine Hydrochloride | 1 |
| 485 | Polymyxin | 1 |
| 486 | Posaconazole | 3c,4d |
| 487 | Pramipexole | 3b |
| 488 | Prasterone + Estradiol Valerate | 3d |
| 489 | Pravastatin Sodium | 3d |
| 490 | Prazepam | 3 |
| 491 | Prednisolone + Neomycin | 1 |
| 492 | Pregabalin | 3a,4d |
| 493 | Prifinium Bromide | 3 |
| 494 | Primidone | 3e |
| 495 | Progesterone | 3d |
| 496 | Progestogen Oral Contraceptive | 3 |
| 497 | Proguanil Hydrochloride + Atovaquone | 3 |
| 498 | Propafenone Hydrochloride | 3e |
| 499 | Propantheline Bromide | 3d |
| 500 | Propofol | 3 |
| 501 | Propranolol Hydrochloride | 3 |
| 502 | Propyphenazone + Butalbital + Caffeine | 3 |
| 503 | Propyphenazone + Codeine | 3d |
| 504 | Pyrantel Pamoate | 3 |
| 505 | Pyrimethamine + Sulfamethoperazine | 2,3 |
| 506 | Quetiapine | 3a |
| 507 | Quinapril + Diuretics | 3b |
| 508 | Quinapril | 3b |
| 509 | Quinine | 2,4 |
| 510 | Quinupristin + Dalfopristin | 3c |
| 511 | Rabbit Anti-Human Thymocyte Immunoglobulin | 3 |
| 512 | Rabeprazole Sodium | 3b |
| 513 | Ramipril | 3d |
| 514 | Ramipril + Diuretics | 3d |
| 515 | Ranitidine | 3d |
| 516 | Raubasine | 3d |
| 517 | Reboxetine | 3b |
| 518 | Remifentanil | 3 |
| 519 | Resagiline | 3b |
| 520 | Reserpine + Chlorthalidone | 3 |
| 521 | Reserpine + Dihydroergocristine + Clopamide | 3 |
| 522 | Ribavirin | 2b,3b |
| 523 | Rifampicin | 3 |
| 524 | Rifampicin + Isoniazid | 3 |
| 525 | Riluzole | 3c |
| 526 | Risedronate | 2,3 |
| 527 | Risperidone | 3c |
| 528 | Ritonavir | 3b |
| 529 | Rivastigmine | 3a |
| 530 | Rizatriptan | 3b |
| 531 | Ropinirole | 3b |
| 532 | Rosiglitazone Maleate | 3b |
| 533 | Rosuvastatin | 3b |
| 534 | Roxatidine Acetate Hydrochloride | 3e |
| 535 | Roxithromycin | 3e |
| 536 | Rufloxacin Hydrochloride | 3b |
| 537 | Salmeterol | 3 |
| 538 | Salmon Calcitonin | 3c |
| 539 | Salt Morphine | 3d |
| 540 | Saquinavir | 3 |
| 541 | Scopolamine Hydrobromide | 3d |
| 542 | Scopolamine Methylbromide/ Diazepam | 3 |
| 543 | Selegiline Hydrochloride | 3b |
| 544 | Sertraline | 3a |
| 545 | Sildenafil | 3b |
| 546 | Simvastatin + Ezetimibe | 3d |
| 547 | Simvastatin | 3d |
| 548 | Sodium Neridronate | 3b |
| 549 | Sodium Nitroprusside | 3 |
| 550 | Sodium Oxybate | 3b |
| 551 | Sodium Stibogluconate | 3 |
| 552 | Somatostatin | 3 |
| 553 | Sorafenib | 2b |
| 554 | Sotalol Hydrochloride | 3b |
| 555 | Spectinomycin Hydrochloride | 3 |
| 556 | Stavudine | 3b |
| 557 | Streptomycin | 1 |
| 558 | Sucralfate | 3c |
| 559 | Sulfadiazine | 2,3 |
| 560 | Sulfametoxazolo + Trimethoprim | 2e,3e |
| 561 | Sulfasalazine | 2d,3d |
| 562 | Sulindac | 2b,3b |
| 563 | Sumatriptan | 3b |
| 564 | Sunitinib | 3b |
| 565 | Tacrolimus | 3b,4b |
| 566 | Tadalafil | 3 |
| 567 | Tamsulosin Hydrochloride | 3b |
| 568 | Teicoplanin | 1e,2e, 3e |
| 569 | Telithromycin | 3c |
| 570 | Telmisartan + Diuretics | 3b |
| 571 | Telmisartan | 3c |
| 572 | Temazepam | 3 |
| 573 | Tenofovir Disoproxil | 3a |
| 574 | Tenoxicam | 2,3c |
| 575 | Terazosin | 3b |
| 576 | Terbinafine | 3 |
| 577 | Teriparatide | 3b |
| 578 | Terlipressin | 3 |
| 579 | Tetanus Vaccine | 3e |

| | | |
|---|---|---|
| 580 | Thiamine + Pyridoxine + Hydroxocobalamin | 3 |
| 581 | Thiopental Sodium | 3 |
| 582 | Thyrotropin Alfa | 3b |
| 583 | Tiagabine | 3a |
| 584 | Tiaprofenic Acid | 2,3 |
| 585 | Tibolone | 3e |
| 586 | Ticlopidine Hydrochloride | 3 |
| 587 | Tigecicline | 3b |
| 588 | Timolol + Pilocarpine Hydrochloride | 2 |
| 589 | Timolol Maleate | 2,3 |
| 590 | Tinidazole + Nystatin | 3 |
| 591 | Tinidazole | 3 |
| 592 | Tiotropium | 3c |
| 593 | Tipranavir | 3c |
| 594 | Tizanidine | 3 |
| 595 | Tobramycin | 1 |
| 596 | Tobramycin + Dexamethasone | 1 |
| 597 | Topiramate | 3b |
| 598 | Toremifene | 3d |
| 599 | Torsemide | 1e,2e |
| 600 | Tramadol | 3a |
| 601 | Trandolapril | 3 |
| 602 | Trandolapril + Calcium Channel Blockers | 3b |
| 603 | Tranexamic Acid | 3 |
| 604 | Tranylcypromine + Trifluoperazine | 3 |
| 605 | Trapidil | 3e |
| 606 | Trastuzumab | 3b |
| 607 | Trazodone Hydrochloride | 2e,3e |
| 608 | Tretinoin | 3a,4a |
| 609 | Triamcinolone | 3 |
| 610 | Triazolam | 3 |
| 611 | Trihexyphenidyl Hydrochloride | 3 |
| 612 | Trimetazidine Dihydrochloride | 3e |
| 613 | Trimipramine | 2b,3b |
| 614 | Triptorelin | 3 |
| 615 | Tropicamide | 3 |
| 616 | Tropisetron | 3 |
| 617 | Urapidil Hydrochloride | 3e |
| 618 | Valacyclovir | 3c |
| 619 | Valgancyclovir | 3b |
| 620 | Valsartan + Diuretics | 2c,3d |
| 621 | Vancomycin | 1d |
| 622 | Vardenafil | 3b |
| 623 | Varenicicline | 2,3 |
| 624 | Varicella Virus Vaccine Live | 3e |
| 625 | Venlafaxine | 2b,3b |
| 626 | Verapamil Hydrochloride | 3b |
| 627 | Vigabatrin | 3 |
| 628 | Viminol-P-Hydroxybenzoate | 3e |
| 629 | Vinblastine Sulphate | 1d |
| 630 | Vincristine Sulphate | 1 |
| 631 | Vindesine Sulphate | 1 |
| 632 | Vinorelbine | 1 |
| 633 | Voriconazole | 2d,3b, 4d |
| 634 | Warfarin Sodium | 3d |
| 635 | Zaleplon | 3c,4c |
| 636 | Zidovudine | 3 |
| 637 | Zidovudine + Lamivudine | 3d |
| 638 | Zoledronate | 3c |
| 639 | Zolmitriptan | 3b |
| 640 | Zolpidem Tartrate | 3,4 |
| 641 | Zonisamide | 3a |
| 642 | Zopiclone | 3 |

## Acknowledgements

This work has been supported by A.I.R.S. Onlus, the Italian Association for Research on Deafness. We wish to thank the Italian Medicines Agency (AIFA) for their collaboration and bibliography support.

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