

RESPIRATORY DISEASES

Respiratory diseases are very common. Chronic obstructive pulmonary disease (COPD) and bronchial asthma are among the most prevalent chronic diseases, and a frequent cause of morbidity and premature deaths worldwide.

Idiopathic pulmonary fibrosis (IPF) is a rare disease which is severely debilitating and ultimately lethal.

COPD

COPD is a chronic disease of the lungs that causes coughing, excessive mucus production and inflammation and ultimately destroys the lung tissue. The alveoli and thus gas exchange are the most affected. This leads to a limitation of airflow, causing shortness of breath and other respiratory symptoms. The airflow limitation is only partially reversible and usually worsens over time leading to disability and ultimately to death. Symptoms such as excess cough and breathlessness are the main reasons why COPD is very stressful for patients. Lung emphysema and chronic bronchitis are the main manifestations of COPD.

COPD is caused by continuous damage to the lungs resulting from inhaling pollutants, primarily cigarette smoke. However, other factors also need to be considered including indoor and outdoor air pollution. The course of COPD, which is a disease that occurs in the second half in a human's life, is characterised by an accelerated loss of lung function compared to normal ageing and occasional sudden worsening of symptoms and function – referred to as acute exacerbations. This can lead to a downward spiral of worsening symptoms and thus further inactivity.

Bronchial asthma

Bronchial asthma is a chronic inflammatory disorder of the airways. The inflammation is accompanied by airway hyperresponsiveness, which leads to a narrowing of the airways and recurrent episodes of wheezing, breathlessness and coughing. These symptoms occur particularly at night or in the early hours of the morning. It is now known that asthma can be triggered by genetic and environmental factors (e.g. allergens and viral infections). Unlike COPD, asthma can occur very early in childhood; it can also be present in adolescents or adults. Asthma is often underestimated as an easy-to-manage condition. However, almost one in two patients with asthma still experience symptoms while receiving maintenance therapy, putting them at increased risk of potentially life-threatening asthma exacerbations.

INDICATIONS	BRAND NAMES	ACTIVE INGREDIENTS	
- Chronic obstructive pulmonary disease (COPD)	SPIRIVA® SPIRIVA® HANDIHALER® SPIRIVA® RESPIMAT®	<i>tiotropium bromide</i>	 <p>Maintenance treatment of patients with COPD (including chronic bronchitis and emphysema), maintenance treatment of associated dyspnoea and for prevention of exacerbations.</p>
- Bronchial asthma	SPIRIVA® RESPIMAT®	<i>tiotropium bromide</i>	 <p>An add-on maintenance treatment in adult patients with asthma who are currently treated with the maintenance combination of inhaled corticosteroids.*</p> <p><i>*Spiriva® Respimat® is approved for use in asthma in the EU, Japan, the USA and many other countries. The label varies by country. Please refer to the local product information.</i></p>
- Chronic obstructive pulmonary disease (COPD)	SPIOLTO® RESPIMAT® STIOLTO® RESPIMAT® INSPIOLO® RESPIMAT®	<i>tiotropium bromide, olodaterol hydrochloride</i>	 <p>Maintenance treatment of airflow obstruction in patients with chronic obstructive pulmonary disease (COPD).</p>
- Chronic obstructive pulmonary disease (COPD)	STRIVERDI® RESPIMAT®	<i>olodaterol hydrochloride</i>	 <p>Maintenance treatment of patients with chronic obstructive pulmonary disease (COPD).</p>
- Reversible bronchospasms associated with obstructive airway diseases	COMBIVENT® RESPIMAT®	<i>ipratropium bromide, salbutamol, sulphate</i>	 <p>A combination of a short-acting anticholinergic and beta-adrenergic for the management of reversible bronchospasms associated with obstructive airway diseases in patients requiring more than one bronchodilator.</p>
- Chronic obstructive pulmonary disease (COPD) - Chronic bronchitis - Bronchial asthma	ATROVENT®	<i>ipratropium bromide</i>	 <p>Prevention and treatment of shortness of breath in patients with chronic obstructive pulmonary disease (COPD) and mild to moderate bronchial asthma in adulthood and childhood as a supplement to beta-agonists in cases of acute asthma.</p>
- Chronic obstructive airway disorders	BERODUAL® BRONCHODUAL® DUOVENT®	<i>ipratropium bromide, fenoterol hydrobromide</i>	 <p>Prevention and treatment of symptoms in chronic obstructive airway disorders with reversible airflow limitation such as bronchial asthma and especially chronic bronchitis with or without emphysema.</p>

RESPIRATORY DISEASES (CONTINUED)

Idiopathic pulmonary fibrosis (IPF)

IPF is a progressive lung disease associated with a markedly reduced life span and affecting as many as 14-43 people per 100,000 worldwide. IPF is characterised by progressive scarring of lung tissue and a loss of lung function over time. Development of scarred tissue is called fibrosis. Over time, as the tissue thickens and stiffens with scarring, the lungs lose their ability to take in and transfer oxygen into the bloodstream, and vital organs do not get enough oxygen. As a result, individuals with IPF experience shortness of breath, even when resting, and often have difficulty participating in everyday physical activities.

Acute IPF exacerbations are defined as rapid deteriorations of symptoms and lung function within days or weeks. These events can occur at any point in the course of the disease, even at first presentation, and are associated with high mortality. All patients with IPF are at risk of acute IPF exacerbations.

INDICATIONS	BRAND NAMES	ACTIVE INGREDIENTS	
<p>- Bronchial asthma</p>	<p>BEROTEC®</p>	<p><i>fenoterol hydrobromide</i></p>	<p>Symptomatic treatment of acute asthma attacks.</p> <p>Prophylaxis of exercise-induced asthma bronchiale.</p> <p>Symptomatic treatment of allergic and non-allergic asthma bronchiale and other conditions with reversible airway narrowing, e.g. chronic obstructive bronchitis.</p> 
<p>- Bronchial asthma - Allergic rhinitis</p>	<p>ALESION® FLURINOL®</p>	<p><i>epinastine hydrochloride</i></p>	<p>Prophylactic treatment of patients with bronchial asthma. Prophylaxis and symptomatic treatment of allergic rhinitis.</p> 
<p>- Idiopathic pulmonary fibrosis (IPF)</p>	<p>OFEV®</p>	<p><i>nintedanib esylate</i></p>	<p>Treatment of patients with idiopathic pulmonary fibrosis (IPF).</p> 

CARDIOVASCULAR AND METABOLIC DISEASES

Cardiovascular (CV) disease is the leading cause of death in many countries and is still increasing in prevalence. Currently it is responsible for nearly one in three deaths worldwide. One key risk factor for developing cardiovascular disease is the presence of diabetes: people with diabetes are two to four times more likely to develop cardiovascular disease than people without diabetes, and as a result, their life expectancy is up to 12 years shorter. Proper control of diabetes and other treatable risk factors is therefore vital for the prevention of cardiovascular events.

Stroke

Stroke is the rapidly developing loss of brain functions caused by a reduced blood flow to the affected brain tissue. This can be due to ischaemia (lack of blood supply) caused by thrombosis or embolism, or due to a bleeding. As a result, the affected area of the brain is unable to function and the damage quickly becomes permanent, if untreated. A stroke is an acute event requiring emergency diagnosis and intervention. Worldwide, stroke is one of the leading causes of death and long-term disability. Symptoms of a transient ischaemic attack (TIA) are similar to stroke, but last for only a few minutes or hours and usually do not result in permanent neurological damage. As a TIA may precede a stroke, emergency medical care and subsequent preventive treatment may be necessary.

Atrial fibrillation

Atrial fibrillation (AF) is the most common sustained heart rhythm condition, affecting approximately two per cent of the total population. One in four adults over 40 develops the arrhythmia in their lifetime. Patients with AF are at higher risk of developing blood clots in their upper left heart chamber, which can cause a disabling stroke if the clot breaks loose and travels to the brain. AF leads to a five-fold increase in the risk of stroke, resulting in up to three million patients worldwide suffering AF-related strokes each year. The risk of stroke can be reduced by effective chronic anticoagulation.

Prevention and treatment of venous thromboembolism

Venous thromboembolism (VTE) is an umbrella term that encompasses deep vein thrombosis (DVT) and pulmonary embolism (PE). DVT is a process that occurs when a thrombus (blood clot) forms in a deep vein, most commonly in the calf or leg, and partially or completely blocks the flow of blood. As the thrombus grows, a portion may break away from the main clot and travel in the circulatory system to the lungs. The lodging of a blood clot in the arteries of the lung is called a PE. VTE is a serious disorder with potentially fatal consequences.

Patients undergoing orthopaedic surgery are at considerable risk of developing VTE, and chronic venous insufficiency and/or pulmonary hypertension may develop in the longer term. To prevent VTE events and their consequences after orthopaedic surgery, patients should receive some kind of thromboprophylaxis. Patients who have already suffered from VTE require anticoagulant treatment for secondary prevention of a recurrent thromboembolic event.

Reversing anticoagulation

Anticoagulants offer important benefits to patients at risk of thromboembolic events. However, even though rare, there will be situations when rapid reversal of anticoagulation could be medically necessary, e.g. if a patient taking an anticoagulant is involved in a severe car accident and needs emergency surgery.

INDICATIONS	BRAND NAMES	ACTIVE INGREDIENTS	
<ul style="list-style-type: none"> - Stroke prevention in atrial fibrillation - Primary prevention of venous thromboembolic events after orthopaedic surgery - Treatment and secondary prevention of venous thromboembolic events 	PRADAXA® PRADAXAR® PRAZAXA®	<i>dabigatran etexilate</i> 	<p>Prevention of strokes and blood clots in patients with abnormal heart rhythm (atrial fibrillation).</p> <p>Primary prevention of venous thromboembolic events (VTE) in adults after elective total hip or knee replacement surgery.</p> <p>Treatment of deep vein thrombosis (DVT) and pulmonary embolism (PE), and secondary prevention of recurrent DVT and PE in adults.</p>
<ul style="list-style-type: none"> - Specific reversal of PRADAXA® (dabigatran etexilate) 	PRAXBIND®	<i>idarucizumab</i> 	<p>PRAXBIND® is a specific reversal agent for dabigatran and is indicated in adult patients treated with PRADAXA® (dabigatran etexilate) when rapid reversal of its anticoagulant effects is required: for emergency surgery/urgent procedures; in life-threatening or uncontrolled bleeding.</p>
<ul style="list-style-type: none"> - Hypertension - Cardiovascular morbidity and mortality prevention 	MICARDIS® MICARDISPLUS® MICARDIS® PLUS MICARDIS®HCT CO-MICARDIS®	<i>telmisartan; telmisartan, hydrochlorothiazide</i> 	<p>Treatment of hypertension. For the reduction of the risk of myocardial infarction (heart attack), stroke or death from cardiovascular (CV) causes in patients 55 years of age or older at high risk of developing major CV events who are unable to take ACE inhibitors (USA).</p> <p>For the reduction of cardiovascular morbidity in patients with manifest atherothrombotic cardiovascular disease (history of coronary heart disease, stroke or peripheral arterial disease), or patients with type 2 diabetes mellitus with documented target organ damage (EU).</p>
<ul style="list-style-type: none"> - Hypertension 	TWYNSTA® MICAMLO® MICARDIS® AMLO MICARDIS® DUO	<i>telmisartan, amlodipine</i> 	<p>Treatment of hypertension alone or with other antihypertensive agents. As initial therapy in patients likely to need multiple antihypertensive agents to achieve their blood pressure goals (USA).</p> <p>Add-on therapy in adult patients with not adequately controlled blood pressure on amlodipine, and replacement therapy in adult patients receiving telmisartan and amlodipine from separate tablets (EU).</p>

CARDIOVASCULAR AND METABOLIC DISEASES (CONTINUED)

Hypertension and cardiovascular diseases

Hypertension, also referred to as high blood pressure, is a chronic disease in which the blood pressure is chronically elevated. Hypertension is also one of the major risk factors for stroke, heart attacks, heart failure and chronic renal failure. The primary goal of any antihypertensive treatment is to prevent such cardiovascular events and to reduce cardiovascular mortality.

Acute myocardial infarction

An acute myocardial infarction, or heart attack, is an event that occurs when a thrombus or clot suddenly prevents blood flow to an area of the heart muscle. Unless the blood flow is restored quickly, the affected section of heart muscle becomes permanently damaged. Heart attack is a leading cause of death in all developed countries.

INDICATIONS	BRAND NAMES	ACTIVE INGREDIENTS	
<ul style="list-style-type: none"> - Acute ischaemic stroke - Acute myocardial infarction - Acute massive pulmonary embolism - Catheter clearance due to thrombotic occlusion 	ACTILYSE® ACTILYSE® CATHFLO®	<i>alteplase</i>	 <p>Fibrinolytic treatment of acute ischaemic stroke, acute myocardial infarction, acute massive pulmonary embolism. Fibrinolytic treatment of occluded catheters.</p>
<ul style="list-style-type: none"> - Secondary prevention of stroke or transient ischaemic attacks (TIA) 	AGGRENEX® ASASANTIN® ASASANTIN® RETARD	<i>dipyridamole, acetylsalicylic acid</i>	 <p>Prevention of stroke following an initial first stroke, or transient ischaemic attacks (TIA).</p>
<ul style="list-style-type: none"> - Acute myocardial infarction 	METALYSE®	<i>tenecteplase</i>	 <p>Fibrinolytic treatment of acute myocardial infarction.</p>
<ul style="list-style-type: none"> - Hypertension 	CATAPRESAN® CATAPRES® CATAPRESSAN® CATAPRES-TTS®	<i>clonidine; hydrochloride clonidine</i>	 <p>Treatment of hypertension.</p>
<ul style="list-style-type: none"> - Hypertension 	MOTENS®	<i>lacidipine</i>	 <p>Treatment of hypertension.</p>

CARDIOVASCULAR AND METABOLIC DISEASES (CONTINUED)

Diabetes

Type 2 diabetes is a chronic, progressive condition associated with elevated blood sugar levels that can cause long-term complications if not treated.

Every year, 4.9 million deaths worldwide are linked directly to the long-term effects of diabetes. Type 2 diabetes is the most common form of diabetes and accounts for up to 95% of all cases in the developed world: it now affects 415 million people worldwide and is imposing an enormous burden on health care systems globally. Without effective prevention and management strategies, it is estimated that the number of cases will reach 642 million by 2040.

Type 2 diabetes is one of the major risk factors for cardiovascular disease. Life expectancy of people with type 2 diabetes at high cardiovascular risk is, on average, decreased by up to twelve years.

Approximately 50 per cent of deaths in people with type 2 diabetes are caused by cardiovascular disease, indicating a high unmet medical need.

In addition to cardiovascular disease, serious complications of diabetes include: nephropathy, leading to renal failure and potentially dialysis; retinopathy with potential loss of vision; peripheral neuropathy with the risk of foot ulcers and foot and leg amputations; autonomic neuropathy causing gastrointestinal, genitourinary and cardiovascular symptoms and sexual dysfunction.

INDICATIONS	BRAND NAMES*	ACTIVE INGREDIENTS	
- Type 2 diabetes mellitus	TRAJENTA® TRADJENTA® TRAZENTA® TRAYENTA®	<i>linagliptin</i>	 <p>Treatment of type 2 diabetes mellitus to improve glycaemic control in adults, used in monotherapy (if metformin is not tolerated or contraindicated) or in combination therapy.</p>
- Type 2 diabetes mellitus	JENTADUETO® TRAYENTA DUO® TRAJENTA DUO® TRAJENTAMET®	<i>linagliptin, metformin hydrochloride</i>	 <p>Treatment of type 2 diabetes mellitus to improve glycaemic control in adults when treatment with metformin does not lead to sufficient control or when patients are treated with TRAJENTA® (linagliptin) and metformin.</p>
- Type 2 diabetes mellitus	JARDIANCE® JARDIANZ®	<i>empagliflozin</i>	 <p>Treatment of adults with type 2 diabetes mellitus as an adjunct to diet and exercise to improve glycaemic control and to reduce the risk of cardiovascular death in patients with established cardiovascular disease.</p>
- Type 2 diabetes mellitus	SYNJARDY®	<i>empagliflozin, metformin hydrochloride</i>	 <p>Treatment of type 2 diabetes mellitus to improve glycaemic control in adults when treatment with metformin does not lead to sufficient control or when patients are treated with JARDIANCE® (empagliflozin) and metformin.</p>
- Type 2 diabetes mellitus	GLYXAMBI®	<i>empagliflozin, linagliptin</i>	 <p>Treatment of type 2 diabetes mellitus to improve glycaemic control in adults when treatment with both empagliflozin and linagliptin is appropriate (US).</p>

* Diabetes portfolio in collaboration with Eli Lilly and Company.

ONCOLOGY

Cancer is a threat to global health. In 2014, an estimated 14.1 million new cases of cancer were diagnosed worldwide and 8.2 million people died from cancer (Stewart, WHO World Cancer Report 2014). The most common diagnosed cancer types are lung cancer (nearly 14%), breast cancer (almost 12%) and colorectal cancer (approx. 10%).

Lung cancer

Lung cancer refers to malignant abnormal cell growth inside the lung tissue, forming a cluster or tumour. It is the most common cancer with an estimated 1.8 million new cases per year worldwide (2014). Smoking is the primary cause of the disease, contributing to nearly 90% of the cases. Recently, however, the incidence of lung cancer among non-smokers has increased. Lung cancer has a poor prognosis, with 1.6 million deaths per year, representing 20% of all cancer deaths: lung cancer symptoms are unspecific so

that the disease may take many years to appear. Late diagnosis in an advanced stage of the disease results in an often dismal prognosis, with only 10 – 15% of lung cancer patients surviving five years or more following diagnosis.

Lung cancer is more than just one disease. There are different subtypes such as small cell lung cancer (SCLC) and non-small cell lung cancer (NSCLC). More than 10 different molecular genetic aberrations (mutations) present in the tumour have been identified. By focusing on molecular changes that are specific to the respective subtype of lung cancer, targeted therapies have become more effective than other treatments. They show a survival benefit and are at the same time less harmful to normal cells, thereby reducing side effects.

INDICATIONS	BRAND NAMES	ACTIVE INGREDIENTS	
<p>- Non-small cell lung cancer (NSCLC)</p>	<p>GIOTRIF® GILOTRIF®</p>	<p><i>afatinib</i></p>	<p> For the treatment of patients with metastatic non-small cell lung cancer (NSCLC) whose tumours have activating epidermal growth factor receptor (EGFR) mutations. For the treatment of patients with locally advanced or metastatic NSCLC of squamous histology progressing on or after platinum based chemotherapy.</p>
<p>- Non-small cell lung cancer (NSCLC)</p>	<p>VARGATEF®</p>	<p><i>nintedanib</i></p>	<p> Combination therapy with docetaxel for the treatment of adult patients with locally advanced, metastatic or locally non-small cell lung cancer (NSCLC) of adenocarcinoma tumour histology after first-line chemotherapy.</p>

DISEASES OF THE CENTRAL NERVOUS SYSTEM

Mental and neurological diseases such as depression and Parkinson's disease significantly impact patients and their families and are also a substantial burden to society.

Parkinson's disease

Parkinson's disease (PD) is a degenerative disorder of the central nervous system. Patients usually notice motor symptoms like hand tremor (shaking) as their first sign of the disease, which may progress to include shaking of the arms, legs or head. Other motor symptoms that may develop over time include stiffness that often results in loss of facial expression and a gradual slowing or loss of motion, or "freezing". About 30-40% of patients also suffer from non-motor symptoms associated with PD, such as

dementia, depression and sleep disorders. The primary symptoms are the result of a lack of the neurotransmitter dopamine in distinct areas of the human brain.

Restless legs syndrome (RLS)

Restless legs syndrome (RLS) is a common neurological disorder characterised by an uncontrollable urge to move the legs, primarily occurring in the evening and night hours. It is usually accompanied by unpleasant and sometimes painful sensations in the legs as well as disturbed sleep resulting in daytime tiredness or sleepiness. The sensations are felt deep within the legs and are described as creeping, crawling or aching.

INFECTIOUS DISEASES

HIV infection/AIDS

Acquired immune deficiency syndrome (AIDS) is a set of symptoms and infections resulting from the damage to the human immune system caused by the human immunodeficiency virus (HIV). If untreated, infection with HIV progressively reduces the effectiveness of the immune system and leaves individuals susceptible to opportunistic infections and tumours. Babies of infected mothers are at risk of getting the virus during pregnancy, childbirth or breastfeeding.

INDICATIONS	BRAND NAMES	ACTIVE INGREDIENTS	
<ul style="list-style-type: none"> - Parkinson's disease (PD) - Restless legs syndrome (RLS) 	SIFROL® MIRAPEX® MIRAPEXIN® PEXOLA®	<i>pramipexole</i> 	Symptomatic treatment of idiopathic Parkinson's disease. It may be used as monotherapy or in combination with levodopa. Symptomatic treatment of idiopathic moderate to severe restless legs syndrome.
<ul style="list-style-type: none"> - Sleep disorders 	LENDORMIN®	<i>brotizolam</i> 	Short-term treatment of disorders of initiating and maintaining sleep. Insomnia requiring pharmacological intervention.

INDICATIONS	BRAND NAMES	ACTIVE INGREDIENTS	
<ul style="list-style-type: none"> - HIV/AIDS 	VIRAMUNE® VIRAMUNE XR®	<i>nevirapine</i> 	For the combination therapy of HIV-1 infection and (in several countries) for the prevention of mother-to-child transmission of HIV-1 in pregnant women who are not taking antiretroviral therapy at time of labour. Prolonged release tablets for once-daily dosing within combination therapy.
<ul style="list-style-type: none"> - HIV/AIDS 	APTIVUS®	<i>tipranavir</i> 	Indicated for combination antiretroviral treatment of HIV-1-infected patients, co-administered with 200 mg of ritonavir, who are treatment-experienced and infected with HIV-1 strains resistant to more than one protease inhibitor.