INDOLIZINE DERIVATIVES AS PHOSPHOINOSITIDE 3-KINASES INHIBITORS

FIELD OF THE INVENTION

The present invention relates to compounds inhibiting Phosphoinositide 3-kinases (hereinafter PI3K); particularly the invention relates to compounds that are indolizine derivatives, methods of preparing such compounds, pharmaceutical compositions containing them and therapeutic use thereof.

More particularly, the compounds of the invention are inhibitors of the activity or function of the Class I of PI3K and more specifically, they are inhibitors of the activity or function of PI3Kα, PI3Kβ, PI3Kδ and/or PI3Kγ isoforms of the Class I PI3K.

Therefore, the compounds of the invention may be useful in the treatment of many disorders associated with PI3K enzymes mechanisms, such as respiratory diseases including asthma, chronic obstructive pulmonary disease (COPD), idiopathic pulmonary fibrosis (IPF) and cough; allergic diseases including allergic rhinitis and atopic dermatitis; autoimmune diseases including systemic lupus erythematous, rheumatoid arthritis and multiple sclerosis; inflammatory disorders including inflammatory bowel disease; cardiovascular diseases including thrombosis and atherosclerosis; hematologic malignancies; cystic fibrosis; neurodegenerative diseases; pancreatitis; multiorgan failure; kidney diseases; platelet aggregation; cancer; sperm motility; organ transplantation and in particular in transplant rejection; graft rejection; lung injuries; and pain including pain associated with rheumatoid arthritis or osteoarthritis, back pain, general inflammatory pain, post hepatic neuralgia, diabetic neuropathy, inflammatory neuropathic pain, trigeminal neuralgia, central pain and respiratory infections, airways damage, treatment and/or prevention of airway injury in patients with PI3Kδ mutations.

BACKGROUND OF THE INVENTION

In biochemistry, a kinase is a type of enzyme that transfers phosphate groups from high-energy donor molecules, such as ATP, to specific substrates, a process referred to as phosphorylation. Specifically, PI3K enzymes are lipid enzyme kinases that can

or infection (such as whooping cough), asthma, chronic obstructive pulmonary disease (COPD) and idiopathic pulmonary fibrosis (IPF)); viral infections (including viral respiratory tract infections and viral exacerbation of respiratory diseases such as asthma and COPD); non-viral respiratory infections (including aspergillosis and leishmaniasis); allergic diseases (including allergic rhinitis and atopic dermatitis); autoimmune diseases (including rheumatoid arthritis and multiple sclerosis); inflammatory disorders (including inflammatory bowel disease); cardiovascular diseases (including thrombosis and atherosclerosis); hematologic malignancies; neurodegenerative diseases; pancreatitis; multiorgan failure; kidney diseases; platelet aggregation; cancer; sperm motility; transplantation rejection; graft rejection; lung injuries; and pain (including pain associated with rheumatoid arthritis or osteoarthritis, back pain, general inflammatory pain, post hepatic neuralgia, diabetic neuropathy, inflammatory neuropathic pain (trauma), trigeminal neuralgia, central pain and respiratory infections, airways damage, treatment and/or prevention of airway injury in patients with PI3Kδ mutations.

14. Use~~A method~~ according to claim 13 wherein the disorder associated by PI3K enzymes mechanisms is asthma, chronic obstructive pulmonary disease COPD idiopathic pulmonary fibrosis (IPF).