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Assessment of Overall Incidence of Esophagogastric and Swallowing/Choking Adverse Events of Alendronate Tablets

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ABSTRACT

Alendronate sodium is a nitrogen-containing synthetic bisphosphonate used in the treatment and prevention of osteoporosis in postmenopausal women, treatment to increase bone mass in men with osteoporosis, treatment of glucocorticoid-induced osteoporosis and treatment of Paget's disease of bone. Alendronate sodium was approved by US FDA in 2000 later, generic applications was approved by FDA approved in 2008. Adverse reactions were reported voluntarily from a population of uncertain size, it is not always possible to reliably estimate their frequency or establish a causal relationship to drug exposure.The present study was aimed to evaluate the overall incidence of esophagogastric and swallowing/choking adverse events for Alendronate. All case reports with adverse events/reactions reported for Alendronate Sodium from the international birth date between 17-Feb-2004 to 16-Dec-2013 were retrieved from the safety database. The estimated incidence of the relevant adverse events suggestive of esophagogastric and swallowing/ choking in relation to the exposure data is as follows (a) Serious events - 0.0681 events per million patient days or 6.81% and (b) Non-serious events - 0.1431 events per million patient days or 14.31%. The study result have shown that the estimated incidence of the relevant adverse events suggestive of esophagogastric and swallowing/ choking in relation to the exposure data were 6.81 % serious and 14.31 % non-serious.

Key words: Alendronate Tablets, Esophagogastric, Swallowing/Choking Adverse Events, Alendronate Sodium

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INTRODUCTION

Alendronate sodium (synthetic nitrogen-containing bisphosphonate) is a non-hygroscopic white crystalline powder soluble in water, very slightly soluble in alcohol and practically insoluble in chloroform. Chemically, Alendronate sodium is P,P'-(4-amino-1-hydroxybutylidene) bis-phosphonic acid, monosodium salt trihydrate with an empirical formula $C_4H_{12}NO_7P_2 \bullet H_6NaO_3$ (Figure. 1) and formula weight of 325.12[1].

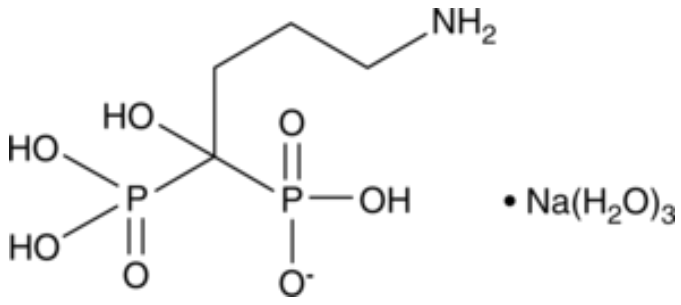

Figure 1: Chemical structure of Alendronate sodium

Alendronate sodium exhibit the following mechanism of action (a) Alendronate have shown preferential localization to sites of bone resorption, exactly under osteoclasts and inhibit osteoclasts activity but does not interfere in the recruitment or attachment of osteoclast. Radioactive [3H] alendronate have shown 10-fold higher uptake on osteoclast surfaces and normal bone was formed on top of the alendronate after 49th day, which was incorporated inside the matrix. Alendronate incorporated in bone matrix was not pharmacologically active. Hence, Alendronate should be continuously administered to suppress osteoclasts on newly formed resorption surfaces. Histomorphometry study in baboons and rats have shown Alendronate treatment reduce the bone turnover (i.e., the number of sites at which bone is remodeled). Additionally, bone formation exceeds bone resorption at these remodeling sites leading to progressive gains in bone mass. Alendronate sodium was indicated for (a) Treatment and prevention of osteoporosis in postmenopausal women, (b) Treatment to increase bone mass in men with osteoporosis, (c) Treatment of glucocorticoid-induced osteoporosis and (d) Treatment of Paget's disease of bone. Alendronate sodium 10 mg daily or 70 mg (tablet or oral solution) once weekly was given as treatment of osteoporosis in postmenopausal women and in men. Alendronate sodium 5 mg daily or 35 mg once weekly was given as prevention of osteoporosis in postmenopausal women. Alendronate sodium 5 mg daily; or 10 mg daily was given as treatment of Glucocorticoid-induced osteoporosis. Alendronate sodium 40 mg daily for six month was given as treatment of Paget's disease. Alendronate sodium was approved by US FDA in 2000 later, generic applications was approved by FDA approved in 2008. Adverse reactions

that have been identified during post-approval use of Alendronate sodium includes urticaria, angioedema, myalgia, malaise, asthenia, fever, hypocalcemia, peripheral edema, esophagitis, esophageal erosions, esophageal ulcers, esophageal stricture or perforation, oropharyngeal ulceration, gastric or duodenal ulcers, osteonecrosis of the jaw, bone pain, joint pain, muscle pain, dizziness, vertigo, acute asthma exacerbations, uveitis, scleritis, episcleritis, rash, pruritus, alopecia, severe skin reactions, Stevens-Johnson syndrome and toxic epidermal necrolysis. However, these reactions are reported voluntarily from a population of uncertain size, it is not always possible to reliably estimate their frequency or establish a causal relationship to drug exposure[1-8.] Hence, the present study was aimed to evaluate the overall incidence of esophagogastric and swallowing/choking adverse events for Alendronate.

MATERIALS AND METHOD

All case reports with adverse events/reactions reported for Alendronate Sodium from the international birth date between 17-Feb-2004 to 16-Dec-2013 were retrieved from the safety database.

RESULTS AND DISCUSSION

For the purpose of this report, four System Organ Classes (SOCs) were selected to identify possible events relevant to esophagogastric and swallowing/ choking events which includes (a) Gastrointestinal disorders, (b) General disorders and administration site conditions, (c) Respiratory, thoracic and mediastinal disorders and (d) Investigations. The MedDRA hierarchy is further analyzed for relevant High Level Group Terms (HLGT), High Level Terms (HLTs) and Preferred Terms (PTs). Fifty nine (Table 1 & Figure.1) unique PTs were selected for final analysis.

Table 1: Summarize the serious and non-serious adverse events/reactions of Alendronate

Preferred Term	Serious	Non-serious
Abdominal discomfort	2	14
Abdominal distension	5	11
Abdominal pain	4	7
Abdominal pain upper	1	28
Abdominal tenderness	0	1
Aphagia	1	1
Aptyalism	1	0
Bronchiectasis	1	0
Chest discomfort	3	3
Chest pain	6	5
Choking	1	1
Choking sensation	1	0
Cough	2	1

Dry mouth	1	3
Dry throat	1	2
Duodenitis	1	0
Dyspepsia	4	17
Dysphagia	11	5
Dysphonia	2	0
Dyspnoea	6	5
Epigastric discomfort	2	0
Eructation	0	3
Gastric disorder	0	3
Gastric pH decreased	1	2
Gastritis	4	2
Gastrointestinal disorder	0	1
Gastrointestinal pain	0	1
Gastrointestinal tract irritation	0	1
Glossitis	2	0
Glossodynia	1	2
Increased upper airway secretion	1	0
Irritability	1	1
Laryngeal ulceration	1	0
Local swelling	5	6
Mucosal erosion	1	0
Mucosal inflammation	0	1
Mucosal ulceration	1	0
Nasal inflammation	0	1
Nausea	5	31
Obstructive airways disorder	1	0
Oesophageal discomfort	0	1
Oesophageal irritation	0	1
Oesophageal pain	0	1
Oesophageal stenosis	7	0
Oesophagitis	1	14
Oesophagitis haemorrhagic	1	0
Oropharyngeal pain	0	7
Pain	250	60
Pharyngeal oedema	1	0
Reflux gastritis	0	1
Regurgitation	0	1
Retching	1	0
Swollen tongue	3	0
Throat irritation	0	8
Throat tightness	3	1
Tongue blistering	0	2
Tongue ulceration	2	0
Upper airway necrosis	1	0
Vomiting	6	5

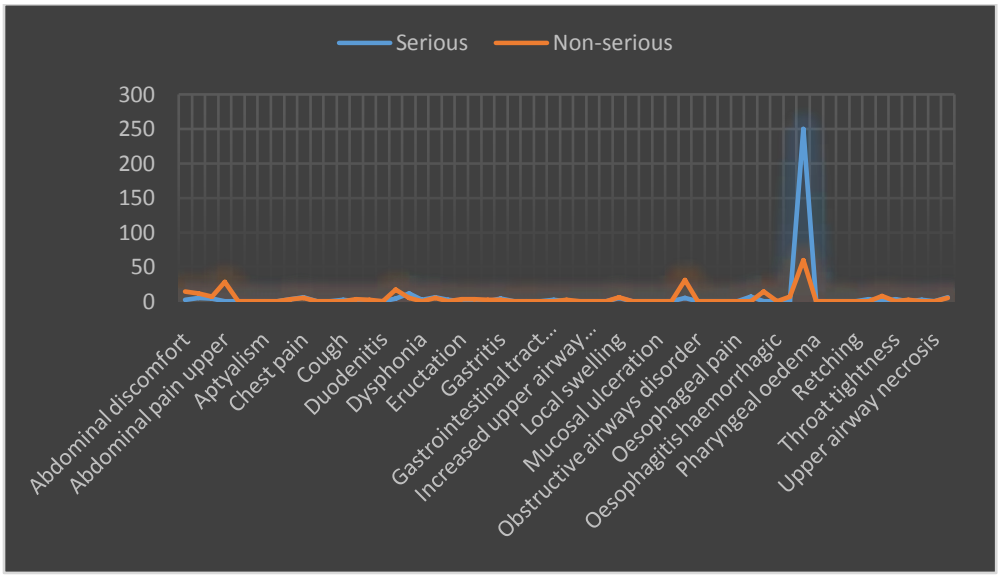

Figure 1: Illustrate the serious and non-serious adverse events/reactions of Alendronate

Exposure data

The exposure data was collected from the previous periodic reports between 17-Dec-2004 to 07-Nov-2013 and the approximate patient exposure days from the launch of the product was 586.86 million days. The incidence of the relevant adverse events is calculated using the formula [(Number of events)/(Number of patient exposure days in millions)] x 100. Based on the above analysis, the estimated incidence of the relevant adverse events suggestive of esophagogastric and swallowing/ choking (Table 2 & Figure. 2) in relation to the exposure data is as follows (a) Serious events - 0.0681 events per million patient days or 6.81% and (b) Non-serious events - 0.1431 events per million patient days or 14.31%.

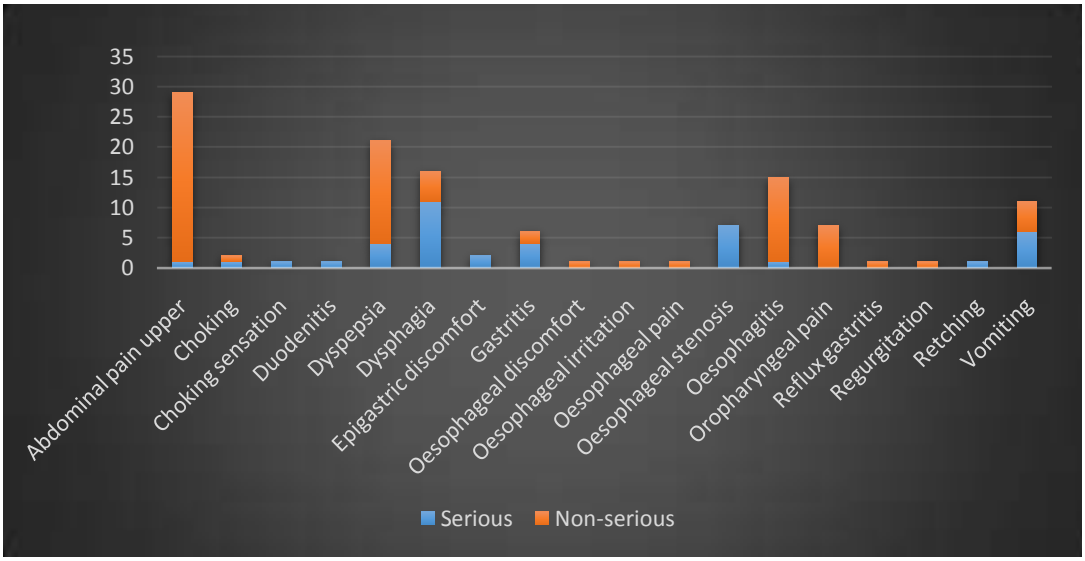

Figure 2: Relevant adverse events of esophagogastric and swallowing/choking of Alendronate

Table 2: Relevant adverse events of esophagogastric & swallowing/choking of Alendronate

Preferred Term	Serious	Non-serious
Abdominal pain upper	1	28
Choking	1	1
Choking sensation	1	0
Duodenitis	1	0
Dyspepsia	4	17
Dysphagia	11	5
Epigastric discomfort	2	0
Gastritis	4	2
Oesophageal discomfort	0	1
Oesophageal irritation	0	1
Oesophageal pain	0	1
Oesophageal stenosis	7	0
Oesophagitis	1	14
Oropharyngeal pain	0	7
Reflux gastritis	0	1
Regurgitation	0	1
Retching	1	0
Vomiting	6	5

CONCLUSION

In the present study, overall incidence of esophagogastric and swallowing/choking adverse events for Alendronate was evaluated. The study result have shown that the estimated incidence of the relevant adverse events suggestive of esophagogastric and swallowing/ choking in relation to the exposure data were 6.81 % serious and 14.31 % non-serious.

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