爲公立醫院的地中海貧血病患者提供的排鐵療法

立法會衞生事務委員會

二零零八年六月二十四日

地中海貧血病

- 地中海貧血病是一種影響紅血球的遺傳性血病，會令人體減少產生健康的紅血球，以致體內紅血球的帶氧量減少
- 需爲重度地中海貧血病患者每數星期輸血一次
- 但輸血後，患者無法自然排出由紅血球所分解的鐵質
- 鐵質會積聚在心臟、肝臟和內分泌腺等內臟， 最終會導致多器官功能障礙
- 需爲患者排去體內積聚的鐵質
- 現有三種排鐵鉗合劑
  - 去鐵胺 (Desferrioxamine)
  - 去鐵酮(Deferiprone)
  - 地拉羅司 (Deferasirox)

醫管局引進藥物

- 須以公平和有效的方法運用公共資源
- 須考慮臨床療效、安全程度、成本效益及機會成本和促進病人的選擇等原則
- 以下三大類藥物須由病人自費購買：
  - 僅具初步醫療驗證的藥物；
  - 與其他替代藥物相比僅具邊際效益的藥物；
  - 生活方式的藥物
- 排鐵藥物在名冊內的定位
  - 去鐵胺及去鐵酮已列入醫管局獲高補貼的標準治療範圍。去鐵胺被列爲普通藥物， 而去鐵酮則被列爲專用藥物。
  - 地拉羅司，列爲自費藥物，屬於具初步醫療驗證和邊際效益的藥物，有報告顯示病人服用後可能出現嚴重副作用及致命併發症

General Information - Chelation therapy

	Desferrioxamine (Desferal ®)	Deferiprone (Ferriprox ®)	Deferasirox (Exjade ®)
Manufacturer	Novartis	Apotex	Novartis
Licensed Indication	Treatment for chronic iron overload	Treatment of iron overload in patients with thalassaemia major when desferrioxamine therapy is contraindicated or inadequate	Treatment of chronic iron overload due to blood transfusions (transfusional haemosiderosis) in patients ≧2 years
Route of administration	Slow subcutaneous infusion over 8-12h, 5-7 times a wk	Oral Three times a day	Oral Once daily
Dosage (licensed age)	20-60mg/kg/day For <3 year (max 40mg/kg) No age limit	25mg/kg three times daily For aged ≥6 year	20-30mg/kg/day For aged ≥2 year
Year on market	>40 years ago	Aug 1999	Nov 2005

Efficacy - Chelation therapy

Desferrioxamine (DFO, Desferal ®)	Deferiprone (Ferriprox ®) vs DFO	Deferasirox (Exjade ®) vs DFO
Current standard Improves hepatic, cardiac and endocrine dysfunction	From Cochrane review - Both deferiprone and DFO significantly reduced iron stores - No evidence to suggest that either was more clinically efficacious - Anecdotal evidence of improved compliance, but Cochrane review found no major diff. in compliance between deferiprone & DFO (all achieved good to excellent compliance).	In randomised non-inferiority, phase 3 1-yr multicentre open-label trial - 52.9% deferasirox (oral 5-30mg/kg) vs 66.4% DFO (sc 20-60mg/kg 5x/wk) responded to treatment - Desferasirox may not have been as effective as DFO. - Only in sub-gp analysis, those with initial high Fe level, iclud. Paed at 30mg/kg/day was found to be comparable to DFO - Deferasirox improves pt satisfaction & quality of life over DFO
Lengthens survival	No data on long-term outcomes (mortality and end organ damage)	No information on the effects of deferasirox on cardiac iron conc. & dysfunction from large prospective randomised controlled studies Long term safety & efficacy of deferasirox is currently unknown.

Side Effects - Chelation therapy

DFO (Desferal ®)	Deferiprone (Ferriprox ®)	Deferasirox (Exjade ®)
Very Common: Local inj site disorder Arthralgia / myalgia Common: (in pts <3 yr given high dose 60 mg/kg) - growth retardation & bone changes - may due to iron overload or excessive DFO dose, but less risk if ≤40 mg/kg. Rare: Retinal abnormalities, vision loss Tinnitus and hearing loss Very rare: Severe allergic reactions Thrombocytopenia	Very Common: Chromaturia (reddish brown urine) GI symptoms Common: Arthropathy, from mild pain in ≥1 joints to severe arthritis with effusion & sig. disability Agranulocytosis (1.1%) Neutropenia (4.9%) **Post marketing surveillance** Reports of agranulocytosis, some with fatal outcome.	Very common: ↑serum creatinine (33%) GI symptoms (26%) Common: Skin rash (7%) Uncommon: High-freq. hearing loss & early cataracts **Post marketing surveillance** Acute renal failure, some with fatal outcome Cytopenias, include agranulocytosis, neutropenia & thrombocytopenia reported in US; some pts died.

Very Common:>10%; Common:1-10%; Uncommon:0.1-1%; Rare:0.01-0.1%; Very rare <0.01%

NOVARTIS

Important Information about Exjade® (deferasirox)
Tablets for Oral Suspension

IMPORTANT DRUG WARNING

DATE: May 14, 2007

Dear Healthcare Provider (or Doctor):

Novartis is writing to summarize the December 2006 changes made to the **WARNINGS** and **ADVERSE REACTIONS** sections of the Exjade® (deferasirox) Tablets for Oral Suspension prescribing information.

Renal

Cases of acute renal failure, some with a fatal outcome, have been reported following the postmarketing use of Exjade® (deferasirox). Most of the fatalities occurred in patients with multiple co-morbidities and who were in advanced stages of their hematological disorders. Particular attention should be given to monitoring serum creatinine in patients who: are at increased risk of complications, have preexisting renal conditions, are elderly, have co-morbid conditions, or are receiving medicinal products that depress renal function.

Serum creatinine should be assessed in duplicate before initiating therapy to establish a reliable pre-treatment baseline, due to variations in measurements. Serum creatinine should be monitored monthly thereafter. Patients with additional renal risk factors (see above) should be monitored weekly during the first month after initiation or modification of therapy, and monitored monthly thereafter.

Cytopenias (formerly Pancytopenia)

There have been postmarketing reports (both spontaneous and from clinical trials) of cytopenias, including agranulocytosis, neutropenia and thrombocytopenia, in patients treated with Exjade. Some of these patients died. The relationship of these episodes to treatment with Exjade is uncertain. Most of these patients had preexisting hematologic disorders that are frequently associated with bone marrow failure. (See ADVERSE REACTIONS.) In line with the standard clinical management of such hematological disorders, blood counts should be monitored regularly. Interruption of treatment with Exjade should be considered in patients who develop unexplained cytopenia.

Important Information about Exjade® (deferasirox)
Tablets for Oral Suspension

Reintroduction of therapy with Exjade may be considered, once the cause of the cytopenia has been elucidated.

In the U.S. Package Insert for Exjade, the following information has been added to the **ADVERSE REACTIONS** section.

Postmarketing Experience.

The following adverse reactions have been spontaneously reported during post-approval use of Exjade. Because these reactions are reported voluntarily from a population of uncertain size, in which patients may have received concomitant medication, it is not always possible to reliably estimate frequency or establish a causal relationship to drug exposure.

There have been reports of cytopenias, including agranulocytosis, neutropenia and thrombocytopenia, in patients treated with Exjade. Although most of these patients had preexisting hematologic disorders that are frequently associated with bone marrow failure, a contributory role for Exjade cannot be excluded. Cases of acute renal failure have been reported in the context of severe complications relating to the underlying disease. (See WARNINGS.)

Skin and subcutaneous tissue disorders: leukocytoclastic vasculitis, urticaria.
Immune system disorders: hypersensitivity reactions (including anaphylaxis and angioedema).

Financial Impact - Chelation therapy

	Desferrioxamine (Desferal ®)	Deferiprone (Ferriprox ®)	Deferasirox (Exjade ®)
HADF classification	General	Special	Self Financed Item
Daily Cost $ 20kg-60kg body wt	$21.2-$169.4	$42-$168	$174.6 to $814.8
Current no. of pt in HA	403	233	19
Total annual cost to HA if all existing pt switched to Deferasirox	$25.7m to $119.9m	$14.8m to $69.3m	$1.21m to $5.7m

Thank you