巧特欣注射劑
DURATOCIN® Injection 100mcg/ml

衛署藥輸字第025800號
本藥限由醫師使用

〔成分〕

每一毫升含主成分carbetocin 100微克

本品賦形劑成分請詳見〔賦形劑〕。

〔藥物劑型〕

注射液劑

無色透明溶液

〔適應症〕

預防在硬膜外或脊髓麻醉下剖腹產後子宮收縮乏力。

（每安瓿一毫升含主成分carbetocin 100微克之靜脈注射液）

Carbetocin尚未針對產後出血高風險的婦女進行研究。

〔用法用量〕

用量

抽出1毫升內含100微克carbetocin的DURATOCIN®，只能靜脈注射，需在醫院內有適當醫療監督下施打。

兒童族群

無相關數據

用法

在剖腹產嬰兒出生後施打。單一劑DURATOCIN®以超過 1 分鐘的速度，慢慢施打。生產後要儘快施打，最好能在移除胎盤前。DURATOCIN®只能施打一劑，不應再施打更多劑的carbetocin。

〔禁忌症〕

- **嬰兒出生前之懷孕和生產陣痛。**
- Carbetocin**不可用於引產（**induction of labor**）。**
- **對**carbetocin、oxytocin**或任一賦形劑過敏。**
- **肝臟疾病或腎臟疾病。**
- **嚴重心血管疾病。**
- **癲癇。**

〔警告〕

只有在設備良好的產科專科醫院，而且隨時都有經驗豐富且合格的專業人員情況下，才能施打carbetocin**。**

在嬰兒出生前任何一產程都不適宜使用carbetocin**，因為單一劑量注射後，其子宮收縮作用會持續幾小時。這和** oxytocin**停止輸注後，藥物作用會快速降低的現象成明顯對比。**

如果施打carbetocin**後子宮還是持續出血，必須要找出出血的原因。要考慮的原因有：胎盤組織殘留、子宮血塊清除不完全或子宮修復不完全、或凝血異常等。**

Carbetocin**僅供單次施打使用。必須慢慢施打超過1分鐘。如果子宮持續張力不足或收縮乏力，造成大量出血，不應重複給予**carbetocin**，應考慮使用**oxytocin**和/或**ergometrine**等其他治療方式。對於使用額外劑量的**carbetocin**或施打**oxytocin**後子宮持續收縮乏力時，再施打**carbetocin**的情況，目前並沒有研究資料。**

一些動物研究顯示，carbetocin**有一些抗利尿作用，因此無法排除低血鈉症的可能性，尤其是當病患也接受大量靜脈輸注液體時。要能辨識出倦怠、昏昏欲睡和頭痛等初期表徵，以預防抽搐和昏迷。**

一般而言，下列情況下要小心使用carbetocin**：偏頭痛、氣喘和心血管疾病、或對一個已經過度負荷的系統，任何快速添加細胞外水分可能會造成危險的狀態。醫師要仔細衡量過**carbetocin**所可能提供給這些特殊病患的潛在效益後，才能決定施打**carbetocin**。**

罹患子癲和子癲前症的病患要監測血壓的變化。

目前尚未針對妊娠糖尿病的患者執行臨床研究。

目前尚未評估陰道生產後使用carbetocin**的療效。**

〔對開車和使用機器的影響〕

不適用。

〔與其他藥物的交互作用〕

臨床試驗時，carbetocin**曾經和一些止痛劑、解痙藥、硬膜上或脊髓麻醉藥劑一起給予，並沒有觀察到有藥物的交互作用。目前還未進行過專門的交互作用研究。**

因為carbetocin**的結構式相當接近**oxytocin**，所以並不排除會發生已知與**oxytocin**相關的交互作用：當尾椎阻斷麻醉時同時給予預防性的血管收縮劑後，給予**oxytocin 3**到**4**小時，有過嚴重高血壓的報告。**

與ergot-alkaloid**類藥物(例如：**methylergometrine**)合併使用時，**oxytocin**和**carbetocin**可能增強這些藥物的血壓增強作用。如果施打**carbetocin**後再給予**oxytocin**或**methylergometrine**，可能會有累積作用的風險。**

由於prostaglandins**可能影響**oxytocin**的效能，預期也可能對**carbetocin**有相同的影響。因此不建議同時服用**prostaglandins**與**carbetocin**。如需同時服用此兩種藥物，須對患者小心監測。**

一些吸入型麻醉藥物(例如：halothane**和**cyclopropane**)可能會增強低血壓作用，和降低**carbetocin**對子宮的作用。有過報告指出與**oxytocin**同時使用時會有心律不整。**

〔不良反應〕

臨床試驗中，在硬膜上或脊髓麻醉下剖腹產後使用carbetocin**所觀察到的不良反應，與使用**oxytocin**觀察到的不良事件的類型和頻率相同。**

系統器官	非常常見 ≧ 1/10	常見 ≧ 1/100 和＜ 1/10
血液和淋巴系統疾病		貧血
神經系統疾病	頭痛，顫抖	頭暈
血管疾病	低血壓，潮紅	
呼吸、胸腔和縱膈疾病		胸痛，呼吸困難
胃腸疾病	噁心，腹痛	金屬味，嘔吐
皮膚和皮下組織疾病	搔癢	
肌肉骨骼和結締組織疾病		背痛
全身異常和施打部位疾病	感覺發熱	寒顫，疼痛

臨床試驗中偶而有出汗和心跳加速的報告。

〔生殖、懷孕和哺乳〕

懷孕

懷孕期間禁止使用carbetocin**於引產 (請參閱禁忌症一節)。**

哺乳

臨床試驗報告指出，對乳汁分泌沒有明顯的影響。目前已經顯示會有少量的carbetocin**從血漿跑到哺乳婦女的乳汁中(請參閱藥物動力學一節)。**Carbetocin**單一劑注射後，少量**carbetocin**跑到初乳和乳汁中，嬰兒攝食後一般認為會被腸道中的酵素降解。**

〔藥效學〕

藥物治療組別：Oxytocin和類似物。

ATC 碼：H01BB03。

在藥理和臨床性質，carbetocin是長效的oxytocin作用劑。

與oxytocin一樣，carbetocin會選擇性地結合到子宮平滑肌上的oxytocin受體，刺激子宮規律地收縮、增加本來已經有的收縮頻率、和提高子宮肌肉的張力等。

對於產後的子宮，carbetocin能增加子宮自然收縮的速率和力量。施打carbetocin後會迅速開始子宮收縮，能在2分鐘內取得強力收縮。

嬰兒出生後，與需要輸注幾小時的oxytocin相比，靜脈注射單一劑100微克carbetocin就足以維持適度的子宮收縮，可以防止子宮乏力和大量出血。

〔藥物動力學〕

Carbetocin顯示出在靜脈注射後，會呈現二相的排除，在400到800微克劑量範圍內呈現線性的藥物動力學。最終排除半衰期約40分鐘。原型藥物的腎臟清除率很低，低於1%的注射藥物以原型經由腎臟排除。

在5位健康授乳媽媽中，於15分鐘時可以偵測到血漿carbetocin濃度，而於60分鐘內達到1035±218 pg/ml最高血中濃度。乳汁中的最高血中濃度比第120分鐘時的血漿濃度低約56倍。

〔藥物過量〕

無論是否是因為對carbetocin**過敏，**carbetocin**藥物過量可能會造成子宮過度收縮。**

Oxytocin藥物過量引起子宮過度刺激，強力或長時間的子宮收縮可能造成子宮破裂或產後出血。

在嚴重情況下，Oxytocin**藥物過量可能會造成低血鈉症和水中毒，尤其是同時攝取過量液體時。因為**carbetocin**是**oxytocin**的類似物，所以無法排除發生類似事件的可能性。**

Carbetocin藥物過量的治療包括症狀治療和支持性療法。藥物過量的表徵及症狀為須由母體提供氧氣。當水中毒時須限制液體的攝取，應增加排尿以修正電解質不平衡，並且控制抽搐的發生。

〔臨床前安全性數據〕

經由安全性試驗、重複藥物毒性試驗以及基因毒性試驗之臨床前試驗數據顯示，carbetocin對於人類沒有特別的風險。

大鼠的生殖毒性研究顯示，從生產到哺乳第21天每天給藥，下一代的體重增加得比較少。沒有觀察到其他的毒性作用。此適應症並不要求提供生殖和胚胎毒性作用研究。

並無執行致癌性試驗，因為carbetocin只能施打一劑。

〔賦形劑〕

L-methionine、succinic acid、mannitol、調整pH使用之sodium hydroxide及water for injections

〔不相容性〕

因為沒有相容性研究，所以本藥劑不能和其他藥劑混合。

〔儲存〕

將小瓶放在外盒中以防光照。

存放在30℃以下，避免冷凍。

〔包裝數量〕

每一瓶帶有鋁蓋及橡膠塞(type I)之玻璃小瓶(type I glass vials (2R))含有1毫升注射溶液。

每盒內有5小瓶。

〔丟棄的特別預防措施〕

DURATOCIN®只能用於靜脈注射。

只有無顆粒、透明溶液才能使用。

所有未使用過的藥品或廢棄物都要按照當地法規丟棄。

製造廠	包裝廠
Ferring GmbH Wittland 11, D-24109 Kiel Germany	Ferring International Center S.A. Chemin de la Vergognausaz 50, CH-1162 Sanit-Prex, Switzerland

藥商：
輝凌藥品股份有限公司
台北市松江路111號11樓
電 話：(02) 2515-8277

DURATOCIN®

QUALITATIVE AND QUANTITATIVE COMPOSITION

Carbetocin 100 micrograms/ml.

For a full list of excipients, see section LIST OF EXCIPIENTS.

PHARMACEUTICAL DOSAGE FORM

Solution for injection.

A clear colourless solution.

INDICATIONS

Prevention of uterine atony following delivery of the infant by Caesarean section under epidural or spinal anaesthesia.

There is limited specific clinical evidence in women at high risk of postpartum haemorrhage.

POSOLOGY AND METHOD OF ADMINISTRATION

Posology

Withdraw 1 ml of DURATOCIN® containing 100 micrograms carbetocin and administer only by intravenous injection, under adequate medical supervision in a hospital.

Paediatric population

No data available

Method of administration

DURATOCIN® must be administered slowly, over 1 minute, only after delivery of the infant by Caesarean section. It should be given as soon as possible after delivery, preferably before removal of the placenta. No further doses of carbetocin should be administered.

CONTRAINDICATIONS

- During pregnancy and labour before delivery of the infant.
- Carbetocin must not be used for the induction of labour.
- Hypersensitivity to carbetocin, oxytocin or to any of the excipients listed in "LIST OF EXCIPIENTS".
- Hepatic or renal disease
- Serious cardiovascular disorders.
- Epilepsy

SPECIAL WARNINGS AND PRECAUTIONS FOR USE

Carbetocin is intended for use only at well equipped specialist obstetrics units with experienced and qualified staff available at all times.

The use of carbetocin at any stage before delivery of the infant is not appropriate because its uterotonic activity persists for several hours after a single bolus injection. This is in marked contrast to the rapid reduction of effect observed after discontinuation of an oxytocin infusion.

In case of persistent uterine bleeding after administration of carbetocin the cause must be determined. Consideration should be given to causes such as retained placental fragments, inadequate emptying or repair of the uterus, or disorders of blood coagulation.

Carbetocin is intended for single administration only. It must be administered slowly over 1 minute. In case of persisting uterine hypotonia or atony and the consequent excessive bleeding, additional therapy with oxytocin and/or ergometrine should be considered. There are no data on additional doses of carbetocin or on the use of carbetocin following persisting uterine atony after oxytocin.

Animal studies have shown carbetocin to possess some antidiuretic activity and therefore the possibility of hyponatraemia cannot be excluded, particularly in patients also receiving large volumes of intravenous fluids. The early signs of drowsiness, listlessness and headache should be recognised to prevent convulsions and coma.

In general, carbetocin should be used cautiously in the presence of migraine, asthma and cardiovascular disease or any state in which a rapid addition to extracellular water may produce hazard for an already overburdened system. The decision of administering carbetocin can be made by the physician after carefully weighing the potential benefit carbetocin may provide in these particular cases.

Patients with eclampsia and pre-eclampsia should be monitored for changes in blood pressure.

Specific studies have not been undertaken in gestational diabetes mellitus.

The efficacy of carbetocin has not been assessed following vaginal delivery.

EFFECTS ON ABILITY TO DRIVE AND USE MACHINES

Not relevent.

INTERACTION WITH OTHER MEDICAMENTS AND OTHER FORMS OF INTERACTION

During clinical trials, carbetocin has been administered in association with a number of analgesics, spasmolytics and agents used for epidural or spinal anaesthesia, and no drug interactions have been identified. Specific interaction studies have not been undertaken.

Since carbetocin is closely related in structure to oxytocin, the occurrence of interactions known to be associated with oxytocin cannot be excluded: severe hypertension has been reported when oxytocin was given 3 to 4 hours following prophylactic administration of a vasoconstrictor in conjunction with caudal-block anaesthesia.

During combination with ergot-alkaloids, such as methylergometrine, oxytocin and carbetocin may enhance the blood pressure enhancing effect of these agents. If oxytocin or methylergometrine are administered after carbetocin there may be a risk of cumulative exposure.

Since it has been found that prostaglandins potentiate the effect of oxytocin, it is expected that this can also occur with carbetocin. Therefore, it is not recommended that prostaglandins and carbetocin be used together. If they are concomitantly administered, the patient should be carefully monitored.

Some inhalation-anesthetics, such as halothane and cyclopropane may enhance the hypotensive effect and weaken the effect of carbetocin on the uterus. Arrhythmias have been reported for oxytocin during concomitant use.

UNDESIRABLE EFFECTS

The adverse events observed with carbetocin during the clinical trials were of the same type and frequency as the adverse events observed with oxytocin when administered after Caesarean section under spinal or epidural anaesthesia.

System Organ Class	**Very common** ≥ 1/10	**Common** ≥ 1/100 and < 1/10
Blood and the lymphatic system disorders		Anaemia
Nervous system disorders	Headache, tremor	Dizziness
Vascular disorders	Hypotension, flushing	
Respiratory, thoracic and mediastinal disorders		Chest pain, dyspnoea
Gastrointestinal disorders	Nausea, abdominal pain	Metallic taste, vomiting
Skin and subcutaneous tissue disorders	Pruritus	
Musculoskeletal and connective tissue disorders		Back pain
General disorders and administration site conditions	Feeling of warmth	Chills, pain

In the clinical trials sweating and tachycardia were reported as sporadic cases.

FERTILITY, PREGNANCY AND LACTATION

Pregnancy

Carbetocin is contraindicated during pregnancy for the induction of labour (see section CONTRAINDICATIONS).

Breastfeeding

No significant effects on milk let-down have been reported during clinical trials. Small amounts of carbetocin have been shown to pass from plasma into breast milk of nursing women (see section Pharmacokinetics). The small amounts transferred into colostrum or breast milk after a single injection of carbetocin, and subsequently ingested by the infant are assumed to be degraded by enzymes in the gut.

CLINICAL STUDY

PHARMACODYNAMICS

Pharmacotherapeutic group: Oxytocin and analogues

ATC code: H01BB03

The pharmacological and clinical properties of carbetocin are those of a long acting oxytocin agonist.

Like oxytocin, carbetocin selectively binds to oxytocin receptors in the smooth muscle of the uterus, stimulates rhythmic contractions of the uterus, increases the frequency of existing contractions, and raises the tone of the uterus musculature.

On the postpartum uterus, carbetocin is capable of increasing the rate and force of spontaneous uterine contractions. The onset of uterine contraction following carbetocin is rapid, with a firm contraction being obtained within 2 minutes.

A single 100 micrograms intravenous dose of carbetocin administered after the delivery of the infant is sufficient to maintain adequate uterine contraction that prevents uterine atony and excessive bleeding comparable with an oxytocin infusion lasting for several hours.

PHARMACOKINETICS

Carbetocin shows a biphasic elimination after intravenous administration with linear pharmacokinetics in the dose range of 400 to 800 micrograms. The terminal elimination half-life is approximately 40 minutes. Renal clearance of the unchanged form is low, with <1% of the injected dose excreted unchanged by the kidney.

In 5 healthy nursing mothers, plasma carbetocin concentrations were detectable by 15 min and peaked at a maximum of 1035 ± 218 pg/ml within 60 min. Peak concentrations in milk were approximately 56 times lower than in plasma at 120 min.

OVERDOSE

Overdosage of carbetocin may produce uterine hyperactivity whether or not due to hypersensitivity to this agent.

Hyperstimulation with strong (hypertonic) or prolonged (tetanic) contractions, resulting from oxytocin overdose can lead to uterine rupture or postpartum haemorrhage.

Overdosage of oxytocin may lead to hyponatraemia and water intoxication in severe cases, especially when associated with excessive concomitant fluid intake. As carbetocin is an analogue of oxytocin, the possibility of a similar event cannot be excluded.

Treatment of overdosage of carbetocin consists of symptomatic and supportive therapy. When signs or symptoms of overdosage occur oxygen should be given to the mother. In cases of water intoxication it is essential to restrict fluid intake, promote diuresis, correct electrolyte imbalance, and control convulsions that may eventually occur.

PRECLINICAL SAFETY DATA

Non-clinical data reveal no special hazard for humans based on conventional studies of safety pharmacology, repeated dose toxicicology and genotoxicity. A reproductive toxicity study in rats, with daily drug administration from parturition to day 21 of lactation, showed a reduction in offspring body weight gain. No other toxic effects were observed. The indication did not warrant studies on fertility or embryotoxicity.

Carcinogenicity studies have not been performed with carbetocin due to the single dose nature of the indication.

LIST OF EXCIPIENTS

L-methionine

Succinic acid

Mannitol

Sodium hydroxide for pH adjustment

Water for injections

INCOMPATIBILITIES

In the absence of compatibility studies, this medicinal product must not be mixed with other medicinal products.

SPECIAL PRECAUTONS FOR STORAGE

Keep vials in the outer carton, in order to protect from light.

Store below 30°C. Do not freeze.

Nature and contents of container

Type 1 glass vials (2R) with type 1 bromobutyle stoppers with aluminium crimp cap containing 1 ml of solution for injection.

Packs of 5 vials.

SPECIAL PRECAUTIONS FOR DISPOSAL

DURATOCIN® is for intravenous use only.

Only clear solutions practically free from particles should be used.

Any unused product or waste material should be disposed of in accordance with local requirements.

MANUFACTURER:

Ferring GmbH

Wittland 11, D-24109 Kiel Germany

PACKAGER:

Ferring International Center SA

Chemin de la Vergognausaz 50,

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