Prescriber Update

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Contents

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Empagliflozin: advise patients on the risk of ketoacidosis and Fournier's gangrene

Key messages

- Empagliflozin is used in the treatment of type 2 diabetes mellitus, to improve glycaemic control and reduce the risk of cardiovascular events in adults.
- Diabetic ketoacidosis and Fournier's gangrene (necrotising fasciitis of the perineum) are rare, but serious and life-threatening conditions that can occur in patients on empagliflozin treatment.
- Inform patients about these potential adverse effects when initiating empagliflozin, including their signs and symptoms and when to seek medical attention.

Sodium glucose co-transporter 2 (SGLT2) inhibitors, such as empagliflozin, are used in the treatment of type 2 diabetes mellitus to improve glycaemic control and reduce the risk of cardiovascular events in adults.

These medicines have been associated with the serious and sometimes life-threatening conditions of diabetic ketoacidosis (DKA) and Fournier's gangrene (necrotising fasciitis of the perineum).[1] Cases of DKA and Fournier's gangrene have been reported to the Centre for Adverse Reactions Monitoring (CARM) following initiation of empagliflozin.

Diabetic ketoacidosis

The signs and symptoms of DKA are described in Table 1. Patients taking SGLT2 inhibitors are at increased risk of DKA, particularly within the first few months of treatment or peri-operatively.[2,3] In some cases, DKA can be atypical with near normal or only slightly raised blood glucose levels (euglycaemic diabetic ketoacidosis).[2]

Risk factors for DKA in patients being treated with empagliflozin include:[1,4]

- insulin dose reduction
- a low carbohydrate diet
- alcohol abuse
- severe dehydration
- pancreatic disorders, such as a history of pancreatitis or pancreatic surgery
- metabolically stressful events, such as severe infection, myocardial infarction, stroke, surgery, prolonged fasting.

Consider stopping empagliflozin temporarily during an acute illness, particularly if patients are unwell, febrile and not eating or vomiting. Empagliflozin should also be temporarily stopped before undergoing medical procedures or surgery[3,5] – consult local clinical guidelines for advice.

Advise patients to seek medical attention if they experience signs and symptoms of DKA (Table 1).

Table 1: Signs and symptoms of diabetic ketoacidosis (DKA) and what to do

Signs and symptoms	What to do
Can include: • difficulty breathing • nausea • vomiting • anorexia • excessive thirst • abdominal pain • confusion and unusual fatigue or sleepiness • a sweet smell to the breath • a sweet or metallic taste in the mouth • a different odour to urine or sweat. More serious signs and symptoms include: • dehydration • deep gasping breathing • confusion • coma.	**Patient** Seek medical attention if experiencing the signs and symptoms of DKA, regardless of the blood glucose level. **Health care professional** Test blood capillary ketones (urine ketone testing may be unreliable). Suspect DKA in patients with or without hyperglycaemia, who are experiencing symptoms of DKA: • and/or a finger prick capillary blood ketone level is above 1.00 mmol/L • and/or a negative base excess of below -5 mmol/L, indicating metabolic acidosis. Stop empagliflozin and treat the DKA.

Source: New Zealand Formulary (NZF). 2021. *NZF v108: Empagliflozin* 1 June 2021. URL: **nzf.org.nz/nzf_71055** (accessed 25 June 2021).

Fournier's gangrene (necrotising fasciitis of the perineum)

Fournier's gangrene is a necrotising bacterial infection of the perineum. It has been reported in both female and male patients on empagliflozin. Serious outcomes have included hospitalisation, multiple surgeries and death.[1,6]

Advise patients to seek immediate medical attention if they experience pain, tenderness, redness or swelling of the genital or perineal area, particularly with associated fever or malaise. These symptoms can worsen quickly.[6]

Initiate treatment promptly with a broad-spectrum antibiotic and surgical debridement, if necessary.[6]

Discontinue empagliflozin and provide an alternative therapy for glycaemic control.[6]

New Zealand case reports

Up to 30 June 2021, CARM has received:

- three reports of DKA, one of which was reported to be euglycaemic (CARM IDs: 139444, 140085, 140811)
- two reports of Fournier's gangrene (CARM IDs: 140656, 140811).

Empagliflozin was listed as the suspect medicine in all of these reports.

More information

See the following *Prescriber Update* articles for more information:

- **Spotlight on empagliflozin** (December 2020)
- **SGLT2 Inhibitors and diabetic ketoacidosis** (December 2015).

References

1. Boehringer Ingelheim (NZ) Limited. 2019. *Jardiance New Zealand Data Sheet* 4 December 2019. URL: medsafe.govt.nz/profs/datasheet/j/jardiancetab.pdf (accessed 25 June 2021).
2. New Zealand Forumulary (NZF). 2021. *NZF v108: Empagliflozin* 1 June 2021. URL: nzf.org.nz/nzf_71055 (accessed 25 June 2021).
3. bpac^{nz}. 2021. *New diabetes medicines funded: empagliflozin and dulaglutide* March 2021. URL: bpac.org.nz/2021/diabetes.aspx (accessed 25 June 2021).
4. Access Lexicomp Online. 2021. *Empagliflozin: Drug information.* In: *UpToDate* v176.0. URL: uptodate.com/contents/empagliflozin-drug-information (accessed 6 July 2021).
5. New Zealand Society for the Study of Diabetes. 2020. *Periprocedural diabetic Ketoacidosis (DKA) with SGLT2 inhibitor use* January 2020. URL: diabetessociety.com.au/documents/ADS_DKA_SGLT2i_Alert_update_2020.pdf (accessed 16 July 2021).
6. US Food and Drug Administration. 2018. *FDA warns about rare occurrences of a serious infection of the genital area with SGLT2 inhibitors for diabetes* 29 August 2018. URL: fda.gov/drugs/drug-safety-and-availability/fda-warns-about-rare-occurrences-serious-infection-genital-area-sglt2-inhibitors-diabetes (accessed 25 June 2021).

Updated safety information: fingolimod and liver injury

Key messages

- Clinically significant liver injury and cases of acute liver failure requiring liver transplant have been reported in patients treated with fingolimod.
- The fingolimod data sheet has been updated:
  - to require liver function monitoring during and after treatment
  - to include criteria for stopping treatment to prevent serious drug-induced liver injury.

Fingolimod is an immunomodulating drug indicated for the treatment of relapsing multiple sclerosis.[1]

Clinically significant liver injury and cases of acute liver failure requiring liver transplant have been reported in patients treated with fingolimod. Information about these cases has been added to the fingolimod (Gilenya) data sheet.[2]

The data sheet has also been updated with the requirement for liver function monitoring during and after treatment and criteria for stopping treatment to prevent serious drug-induced liver injury, as follows.[2]

- Recent (within the last 6 months) transaminase and bilirubin levels should be available before initiation of treatment. Measure levels periodically while on treatment, until two months after fingolimod discontinuation.
- Promptly measure transaminase and bilirubin levels if the patient reports signs and symptoms of liver injury (such as unexplained nausea, vomiting, abdominal pain, right upper abdominal discomfort, new or worsening fatigue, anorexia, or jaundice and/or dark urine during treatment). In this clinical context, if the patient is found to have an alanine aminotransferase (ALT) greater than three times the reference range and serum total bilirubin greater than two times the reference range, treatment with fingolimod should be interrupted.
- Do not resume treatment unless a plausible alternative aetiology for the signs and symptoms of liver injury can be established.

Refer to the Gilenya data sheet for further information.

Up to 30 June 2021, the Centre for Adverse Reactions Monitoring (CARM) has received four adverse reaction reports of increased hepatic enzymes where fingolimod was the suspect medicine (CARM IDs: 116984, 117025, 118005, 119172).

References

1. New Zealand Formulary (NZF). 2021. *NZF v108: Fingolimod* 1 June 2021. URL: nzf.org.nz/nzf_4808 (accessed 21 June 2021).
2. Novartis New Zealand Limited. 2021. *Gilenya New Zealand Data Sheet* 11 February 2021. URL: medsafe.govt.nz/profs/Datasheet/g/gilenyacap.pdf (accessed 21 June 2021).

MARC's remarks: June 2021 meeting

The Medicines Adverse Reactions Committee (MARC) convened via videoconference on 10 June 2021.

Due to serious skin reactions reported overseas, medicines containing **bufexamac** were referred to the Committee under section 36 of the Medicines Act 1981. Bufexamac is a non-steroidal anti-inflammatory medicine for topical application and is a general sale medicine in strengths 5% or less. The Committee considered that medicines containing bufexamac had an unfavourable risk-benefit profile and recommended to the Minister's delegate that the consent to distribute these medicines be revoked. In addition, the Committee recommended that Medsafe make an application to the Medicines Classifications Committee to review the classification of bufexamac.

The Committee discussed concerns associated with the use of medicines with **boron-containing excipients** in children and a potential impact on fertility later in life. The Committee noted that the evidence for fertility concerns associated with boron use was based on animal studies and appeared to be dose related. The relevance to humans was uncertain. The Committee recommended data sheet updates for medicines with boron-containing excipients to reflect what is known from animal and human studies.

The misuse of **stimulant laxatives** in New Zealand was discussed. The Committee recommended that Medsafe undertake a consultation regarding adding warning and advisory statements on the manufacturers' original pack for all stimulant laxatives.

The Committee considered regulatory options for minimising **opioid** misuse, abuse and dependence in New Zealand. Several regulatory actions were recommended by the Committee, such as updating the data sheets, adding new warning labels, enhanced safety monitoring, and communication activities. The Committee questioned the clinical benefits of dihydrocodeine and its role in pain management and recommended that Medsafe undertake a **risk benefit review**.

See the Medsafe website for the **MARC meeting minutes** and the **reports presented to the MARC**.

Report adverse drug reactions

Reporting adverse reactions contributes to the safety of medicines in New Zealand.

If you think your patient has had an adverse reaction to a medicine, report it to CARM.

Online reporting is easiest.

Recent approvals: new active ingredients or new indications

For the period 16 April 2021 to 15 July 2021.

Recent approvals of medicines with new active ingredients

Trade name (active ingredient)	Dose form and strength(s)	Therapeutic area
Beovu (brolizumab)	Solution for injection 120 mg/mL vial 120 mg/mL pre-filled syringe	Neovascular age-related macular degeneration
COVID-19 Vaccine Janssen* (Ad26.COV2.s)	Suspension for injection $5x10^{10}$ virus particles/0.5 mL	Immunisation to prevent COVID-19 in adults aged 18 years and older

* COVID-19 Vaccine Janssen has provisional approval.

Approved medicines with new indications

Trade Name (active ingredient)	Dose form and strength(s)	New therapeutic area(s)
Biktarvy (bictegravir; emtricitabine; tenofovir alafenamide)	Film coated tablet 50 mg/200 mg/25 mg	HIV-1 infection in paediatric patients weighing at least 25 kg
Cabometyx (cabozantinib)	Film coated tablet 20 mg 40 mg 60 mg	Hepatocellular carcinoma
Comirnaty (COVID-19 mRNA vaccine)*	Concentrate for injection 0.5 mg/mL	Immunisation to prevent COVID-19 in adolescents aged 12 to 15 years old
Dysport (botulinum toxin type A)	Powder for injection 300 U 500 U	Focal spasticity of upper limbs in children aged 2 years and older
Zavicefta (ceftazidime; avibactam)	Powder for infusion 2000 mg/500 mg	Infections in paediatric (aged 3 months and older) patients

* Comirnaty has provisional approval.

See the Medsafe website for:

- more information about these medicines
- data sheets of currently marketed medicines.

WE NEED YOUR HELP!

Please send your reports to CARM for the potential safety issues* listed in the table below.

Medicine(s)	Potential safety issue	Active monitoring ends
Pregabalin	Possible risk of bullous dermatitis and exfoliating skin reactions	30 November 2021

- M² (Medicines Monitoring) is a Medsafe scheme designed to collect more information on potential safety signals for specific medicines.
- Please send your report to CARM (as for any suspected adverse reaction). This can be done even if the reaction happened some time ago. Please include as much information as possible as this helps the medical assessors at CARM to investigate whether the medicine caused the reaction.
- **For further information about M²**, see the Medsafe website.

* The appearance of a possible safety issue in this scheme does not mean Medsafe and CARM have concluded that this medicine causes the reaction.

Reminder: hyperkalaemia caused by amiloride or spironolactone

Key messages

- Hyperkalaemia is a well-established risk of treatment with potassium-sparing diuretics such as spironolactone and amiloride.
- The risk of hyperkalaemia is increased in patients with renal or hepatic impairment, the elderly, and those receiving concomitant medicines that can increase potassium.
- Regular monitoring of serum potassium is recommended.

The Centre for Adverse Reactions Monitoring (CARM) has recently received two reports of severe hyperkalaemia in patients taking spironolactone or amiloride monotherapy. Spironolactone and amiloride are potassium-sparing diuretics that can cause hyperkalaemia.

Spironolactone is indicated for a number of conditions, including congestive heart failure and essential hypertension.[1]

There are currently no approved amiloride monotherapy products in New Zealand. There are approved fixed-dose combination products containing amiloride and furosemide or hydrochlorothiazide. Amiloride can be used for potassium conservation as an adjunct to thiazide or loop diuretic therapy for congestive heart failure and hypertension, or cirrhosis with ascites. It can also be used as monotherapy for oedema.[2]

Monitoring and management of hyperkalaemia

Severe hyperkalaemia is defined as a serum potassium concentration 7.0 mmol/L or greater, or 5.4 mmol/L or greater with symptoms and/or electrocardiogram changes.[3]

Serum potassium levels should be monitored at frequent intervals, especially when therapy is initiated, when dosages are changed or with any illness that may cause renal dysfunction. The incidence of hyperkalaemia is greater in patients with renal impairment and in the elderly.[1,2,4]

Concomitant use with other medicines that can increase potassium is not recommended. Examples of medicines that increase potassium include angiotensin-converting enzyme inhibitors (ACEis), angiotensin receptor blockers (ARBs) and non-steroidal anti-inflammatory drugs (NSAIDs).[1]

Severe hyperkalaemia is associated with fatal cardiac arrhythmias and requires urgent treatment. Discontinue the causative medicine and initiate corrective treatment in secondary care.[1,3]

New Zealand case reports

Up to 30 June 2021, CARM has received a total of 12 reports of hyperkalaemia with spironolactone or amiloride. Some of these cases involved concomitant treatment with ACEis or ARBs.

More information

See the following *Prescriber Update* articles:

- **Medicines and hyperkalaemia** – September 2015
- **Reminder: hyperkalaemia caused by spironolactone and renin-angiotensin system medicine interactions** – September 2016.

References

1. Mylan New Zealand Ltd. 2020. *Spiractin New Zealand Data Sheet* 9 October 2020. URL: medsafe.govt.nz/profs/Datasheet/s/Spiractintab.pdf (accessed 15 July 2021).
2. New Zealand Formulary. 2021. *New Zealand Formulary v109: Amiloride hydrochloride* 1 July 2021. URL: nzf.org.nz/nzf_1037 (accessed 15 July 2021).
3. bpac^{nz}. 2011. A primary care approach to sodium and potassium imbalance. *Best Tests* 12: 2–14. URL: bpac.org.nz/BT/2011/September/imbalance.aspx (accessed 15 July 2021).
4. Lexicomp. 2021. Amiloride: drug information. In: *UpToDate*. URL: uptodate.com/contents/amiloride-drug-information (accessed 26 July 2021).

Consider blood cell wellbeing during valproate therapy

Key messages

- Sodium valproate treatment is associated with adverse haematological effects. Thrombocytopenia is a common adverse reaction, while pancytopenia is an uncommon adverse reaction.
- Blood tests are recommended before starting sodium valproate, periodically during treatment, before surgery, and in the case of spontaneous bruising or bleeding.

The Centre for Adverse Reactions Monitoring (CARM) has recently received two reports (CARM IDs 138863 and 138579) of patients being treated with sodium valproate who experienced thrombocytopenia and pancytopenia, respectively.

This article is a reminder of the haematological adverse reactions associated with sodium valproate treatment, which can range from minor bruising and bleeding to severe reactions such as haemorrhagic stroke or pancytopenia.[1]

Sodium valproate and thrombocytopenia – a common adverse reaction

Thrombocytopenia (low platelet count) has been estimated to occur in 5 to 60 percent of patients taking sodium valproate.[2] Thrombocytopenia is listed as common (frequency rating ≥1/100 and <1/10) in the Epilim data sheet.[3]

The time to onset of thrombocytopenia varied in different studies, from the second week of treatment until 16 months after initiation. Risk factors for thrombocytopenia are female gender and older age. The risk is larger when higher doses are used.[1]

The exact mechanism by which sodium valproate can cause thrombocytopenia is unclear. Two possible explanations which have been suggested are:[2,4]

- peripheral platelet destruction due to formation of autoantibodies against platelets
- decreased production of platelets due to a dose-dependent direct bone marrow toxicity.

Thrombocytopenia is generally reversible with dose reduction or discontinuation of sodium valproate.[1]

Uncommon reactions affecting the blood

Pancytopenia (low red blood cells, white blood cells and platelets) and leukopenia (low white blood cells) with or without bone marrow depression are uncommon blood reactions (frequency rating ≥1/1000 and <1/100 in the data sheet).[3] Neutropenia (low neutrophils) has been reported infrequently and mostly within the first weeks of treatment.[1,2]

Direct suppression of the bone marrow by an idiosyncratic mechanism has been proposed as a mechanism for the most severe haematological adverse reactions (eg, pancytopenia).[5]

New Zealand case reports

Up to 30 June 2021, CARM had received 937 case reports associated with sodium valproate treatment.

Table 1 details some of the reactions reported when sodium valproate was a suspect medicine.

Table 1: Overview of reports of haematological adverse reactions suspected to be caused by sodium valproate

Reaction*	Total No.	Age group (years)						Gender	
		0–20	21–40	41–60	61–80	>81	Unknown	F	M
Thrombocytopenia	26	8	7	6	3	1	1	16	10
Neutropenia	24	4	4	9	4	1	2	14	10
Pancytopenia	7	–	1	2	1	2	1	4	3
Leukopenia	6	–	2	4	–	–	–	3	3

* Note: more than one reaction may have been reported for the same patient.

Keep track of the blood cells

Blood tests (full blood cell count and coagulation tests) are recommended for patients taking sodium valproate:[3]

- before starting sodium valproate therapy
- periodically during treatment
- before surgery
- in case of spontaneous bruising or bleeding.

Spontaneous bruising, bleeding or evidence of a haemostasis/coagulation disorder is an indication for dose reduction or withdrawal of sodium valproate whilst the cause of the coagulation disorder is being investigated.

More information

See the following *Prescriber Update* article for more information on sodium valproate and thrombocytopenia:

- **Drug-induced immune thrombocytopenia** (March 2018).

References

1. UpToDate. *Valproate: Drug information* Topic 10035 Version 454.0. URL: uptodate.com/contents/valproate-drug-information (accessed 2 July 2021).
2. Verrotti A, Scaparrotta A, Grosso S, et al. 2014. Anticonvulsant drugs and hematological disease. *Neurological Sciences* 35(7): 983–93. DOI: 10.1007/s10072-014-1701-0 (accessed 2 July 2021).
3. Sanofi-Aventis NZ Limited. 2021. *Epilim New Zealand Data Sheet* 3 May 2021. URL: medsafe.govt.nz/profs/datasheet/e/Epilimtabsyrliqiv.pdf (accessed 2 July 2021).
4. Buoli M, Serati M, Botturi A, et al. 2018. The risk of thrombocytopenia during valproic acid therapy: A critical summary of available clinical data. *Drugs in R & D* 18(1): 1–5. DOI: 10.1007/s40268-017-0224-6 (accessed 2 July 2021).
5. Acharya S, Bussel JB. 2000. Hematologic toxicity of sodium valproate. *Journal of Pediatric Hematology/Oncology* 22(1): 62–5. DOI: 10.1097/00043426-200001000-00012 (accessed 2 July 2021).

Quarterly summary of recent safety communications

The table below is a summary of recent safety communications to health care professionals and consumers, **published on the Medsafe website**.

Date	Communication	Topic
Weekly	COVID-19	Adverse events following immunisation with COVID-19 vaccines
12/08/2021	Monitoring	Dihydrocodeine: review of risks and benefits
21/07/2021	Alert	Myocarditis and pericarditis - rare adverse reactions to Comirnaty (Pfizer COVID-19 vaccine)
12/07/2021	Dear Healthcare Professional Letter	Supply of Comirnaty COVID-19 Vaccine in New Zealand
9/06/2021	Monitoring	Myocarditis – a potential adverse reaction to Comirnaty (Pfizer COVID-19 vaccine)

Gathering knowledge from adverse reaction reports: September 2021

Adverse reaction reporting is an important component of medicine safety monitoring. Case reports can highlight significant safety issues concerning therapeutic products and their use.

The table below presents a selection of recent informative cases from the Centre for Adverse Reactions Monitoring (CARM) database.

Case details[a,b]	Reaction description and data sheet information[b,c]
CARM ID: 139546 **Age:** 57 **Gender:** Male **Medicine(s):** Cyproterone **Reaction(s):** Meningioma	The patient had been on cyproterone therapy for a number of years. He developed a meningioma that required surgical excision.
	The **Siterone data sheet** states that occurrence of (multiple) meningiomas has been reported in association with longer term use (years) of cyproterone acetate at doses of 25 mg/day and above. If a patient treated with Siterone is diagnosed with meningioma, treatment with Siterone must be stopped. See also the September 2020 *Prescriber Update* article, **Cyproterone acetate and the risk of meningioma**.
CARM ID: 140019 **Age:** 65 **Gender:** Male **Medicine(s):** Azathioprine **Reaction(s):** Acute febrile neutrophilic dermatosis (Sweet syndrome)	The patient was diagnosed with Sweet syndrome (acute febrile neutrophilic dermatosis) which started within two weeks after commencing azathioprine. The patient was treated with corticosteroids and azathioprine was discontinued.
	Sweet syndrome is listed in the **Imuran data sheet**. See also the December 2020 *Prescriber Update* article, **A bitter-Sweet syndrome with potential autoimmune connections**.
CARM ID: 140139 **Age:** 42 **Gender:** Male **Medicine(s):** Hydrocortisone **Reaction(s):** Retinopathy	The patient was prescribed 1% hydrocortisone cream to treat widespread sunburn. Two weeks later the patient experienced blurry vision and was sensitive to bright lights. An ophthalmologist diagnosed central serous chorioretinopathy (CSCR).
	Visual disturbance may be reported with systemic and topical corticosteroid use. The **Hydrocortisone Cream 1% PSM data sheet** recommends referral to an ophthalmologist if a patient presents with symptoms such as blurred vision or other visual disturbances. Possible causes may include cataract, glaucoma or rare diseases such as central serous chorioretinopathy (CSCR), which have been reported after use of systemic and topical corticosteroids. See also the September 2018 *Prescriber Update* article, **Corticosteroids and Central Serous Chorioretinopathy (CSCR)**.

CARM ID: 141272 **Age:** 43 **Gender:** Male **Medicine(s):** Pentamidine **Reaction(s):** Hypoglycaemia	A patient receiving intravenous pentamidine treatment experienced sustained hypoglycaemia that required glucose and glucagon infusions.
	The **Pentacarinat data sheet** recommends that fasting blood glucose measurements should be taken daily during therapy, and at regular intervals after the completion of therapy. Hypoglycaemia is commonly reported in association with pentamidine treatment. The hypoglycaemia may be severe and fatal reactions have been reported. Hyperglycaemia and diabetes mellitus with or without preceding hypoglycaemia may occur up to several months after the cessation of therapy.
CARM ID: 140657 **Age:** 82 **Gender:** Female **Medicine(s):** Carbamazepine **Reaction(s):** Thrombocytopenia, epistaxis	Two weeks after starting carbamazepine, the patient experienced acute severe thrombocytopenia with epistaxis. The patient's platelet count had been normal prior to starting treatment.
	Thrombocytopenia is listed as a common adverse reaction in the **Tegretol data sheet**. Leukopenia is listed as very common adverse reaction. Decreased platelet or white blood cell counts may be transient or persistent. Agranulocytosis and aplastic anaemia are listed as very rare adverse reactions. Complete pre-treatment blood counts, including platelets, should be obtained at baseline, and periodically thereafter. If the white blood cell or platelet count is definitely low or decreased during treatment, the patient and the complete blood count should be closely monitored. Discontinue treatment if any if any evidence of significant bone marrow depression appears.
CARM ID: 140808 **Age:** 9 **Gender:** Male **Medicine(s):** Theophylline **Reaction(s):** Supraventricular tachycardia	The patient was experiencing a severe asthma attack and was being treated with intravenous theophylline. He developed severe supraventricular tachycardia, which did not respond to increasing doses of adenosine but did revert with amiodarone.
	Tachycardia is listed in the **DBL Aminophylline Injection BP data sheet**. Aminophylline may antagonise the cardiovascular effects of adenosine by blocking of adenosine receptors.

Notes:

a. Only the medicines suspected to have caused the reaction are listed in the table.

b. The reactions listed in the 'Case details' column are coded according to the Medical Dictionary for Regulatory Activities (MedDRA), an internationally used set of standardised terms relating to medical conditions, medicines and medical devices. The reactions listed in the 'Reaction description' column are based on what was reported to CARM, and do not always match the MedDRA term.

c. If the suspect medicine's brand name is not described in the report to CARM, only the data sheet for the funded medicine is included in the table.

Information about suspected adverse reactions reported to CARM is available on the Medsafe website using the **Suspected Medicines Adverse Reaction Search (SMARS)**.

By selecting the ingredient of a medicine, you can find out:

- the number of reports and suspected adverse reactions for that ingredient. The suspected reactions are grouped by body system or organs (Summary report)
- single case reports, listing the medicines involved that contain the ingredient and the suspected adverse reactions (Detail report).

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The Medicines Classification Committee (MCC) makes recommendations to the Minister of Health on the classification of medicines. Regular emails are sent out that will let you know when the MCC meeting agendas are published, when and how to comment on submissions for reclassification of medicines, when the meeting minutes are published, and when and how to object to a recommendation made by the MCC.

To subscribe, email **committees@health.govt.nz** with the words 'classification — subscribe' in the subject line.

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