DENGUE FACTSHEET

WHAT IS DENGUE, HOW IS IT SPREAD?

- According to the World Health Organization (WHO), **dengue is the most prevalent and rapidly spreading** mosquito-borne viral disease worldwide[1-4]
- Dengue is transmitted by mosquitoes mainly of the species ***Aedes aegypti*** and ***Aedes albopictus***[5]
- Infected Aedes mosquitoes can transmit each of the four different dengue virus serotypes[5] - this means **travellers could be at risk of contracting dengue more than once**[5,6]

WHERE IS DENGUE PREVALENT?

- The risk of dengue is now present in **more than 125 countries**[5]
- **Cases have been confirmed** in European travellers returning from South America, North America, The Caribbean, Africa, Asia and from within Europe itself[7,8]
- Since 2010, over 20 autochthonous dengue outbreaks have been **reported in mainland Europe**[7,9]
- There were ~**105 million reported dengue cases** across the world in 2017 – and dengue is on the rise[10,11]
- Each year, dengue causes an estimated **390 million infections** and more than 20,000 deaths globally[2,5]

WHAT ARE THE RISKS TO TRAVELLERS?

- Dengue infections are rising in European travellers returning from endemic countries[5,12]
- Dengue can be present year round in certain endemic countries, including some with conditions that may be popular with travellers, such as (but not limited to):[1,2,5,13,14]

Urban and rural areas

Areas of high population density

Areas with warmer ambient temperatures (especially 26–29°C)

Indoor and outdoor locations throughout the day

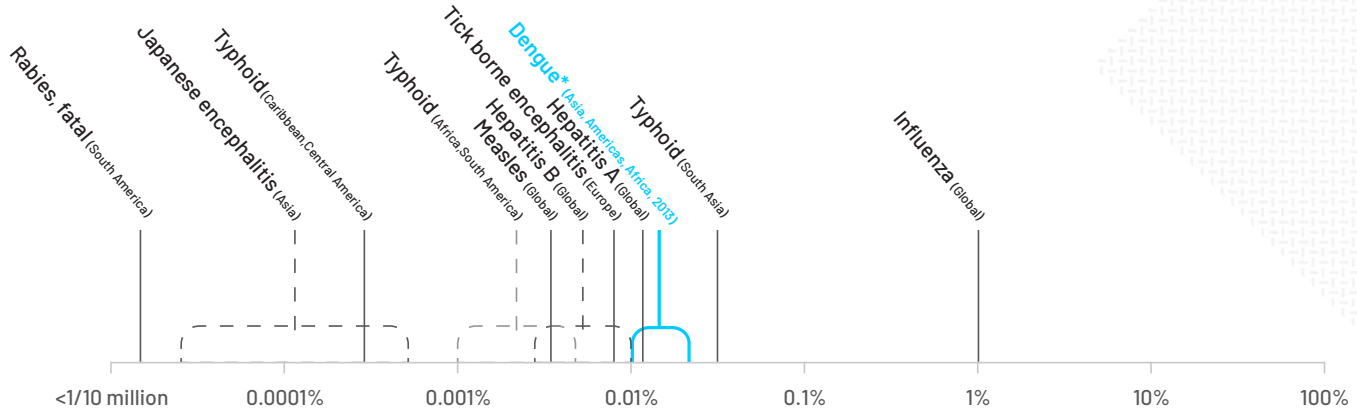
- Dengue can affect people of all ages and ethnicities,[15] however, some may be at a higher risk of developing severe dengue than the general population, such as:

People previously infected with dengue[6]

People with underlying medical conditions[6]

Age, especially the elderly, and certain ethnic groups[6,16]

- When compared to other diseases that travellers are regularly vaccinated against, there may be a higher risk of contracting dengue[14,17,18]



Estimated monthly incidence of vaccine-preventable disease in unvaccinated travellers

Figure adapted from Steffen R *et al. J Travel Med*. 2018;25(1):1-3.
*Diseases positioned by Prof Steffen's personal assessment. Dengue incidence per month calculated as per Ratnam I *et al. Journal of Travel Medicine*. 2013;20(6):384–393, by dividing 1,000 person-months by 1,000 (study period 1991-2010).

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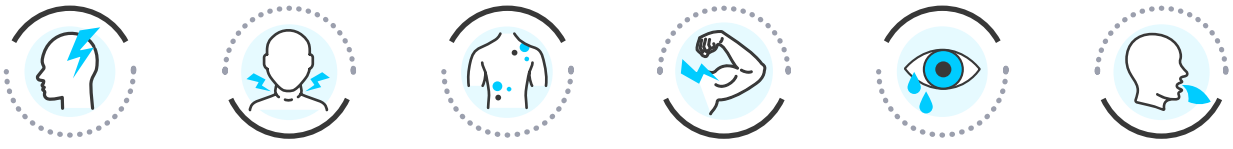
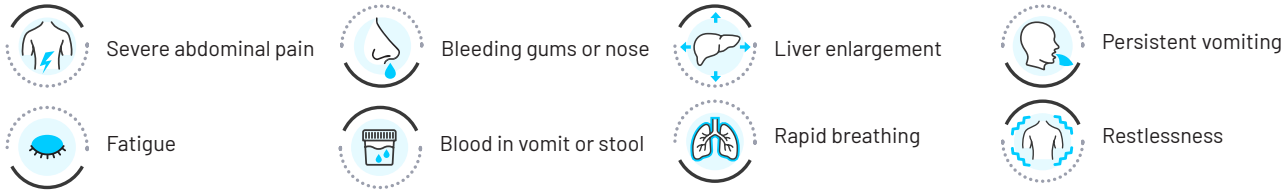
HOW SEVERE IS DENGUE?

- While an estimated 75% of dengue infections may be asymptomatic, symptomatic individuals typically present with a mild to moderate acute febrile illness[7, 19]
- Around 5% of cases can progress to severe dengue[19] which can occasionally lead to hospitalisation[5]
- According to the World Health Organization, high fever and any 2 of the below symptoms could indicate dengue:[5]



Severe headache | **Swollen glands** | **Rash** | **Muscle and joint pains** | **Pain behind the eyes** | **Nausea and Vomiting**

- Severe dengue is a rare and potentially lethal variant of dengue, manifesting as a sudden deterioration of symptoms due to plasma leaking, fluid accumulation, respiratory distress, severe bleeding, or organ impairment[5,14]
- Warning signs of severe dengue include:[5]



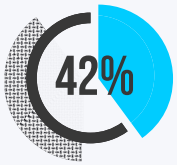
Severe abdominal pain | Bleeding gums or nose | Liver enlargement | Persistent vomiting

Fatigue | Blood in vomit or stool | Rapid breathing | Restlessness

As symptoms can be diverse, laboratory or point-of-care diagnostics are often recommended alongside assessment of clinical presentation to achieve an accurate diagnosis.[20]

REPORTED ILLNESS IN TRAVELLERS

A US based study has revealed that approximately 42% of returning travellers who contracted dengue were hospitalised (n=2119/5009), of which <1% (n=46/5009) of these patients had severe dengue[21]



From 2007-2013, studies reported dengue as being the leading cause of febrile illness among ill travellers returning from Southeast Asia, Latin America and the Caribbean[12]

Approximately 1% (n=46/5009) of travellers who were infected developed severe dengue; it was fatal in about 0.3% (n=18/5009) of cases (2010–2017)[21]

Even short stays in dengue-endemic areas are associated with a **risk of becoming infected**, which increased with longer stays and return travel to endemic areas[14]

PREVENTION MEASURES FOR TRAVELLERS

Personal measures:[22,23]

Indoors, travellers can use **screens** on windows and doors and **bed nets** to help keep mosquitoes away

Wear loose and protective clothing, and apply insect **repellent** to all areas of exposed skin

Before travelling, consider getting **vaccinated** against dengue

Environmental measures:[22,24,25]

Where possible, use **air conditioning**

Keep water containers **clean and empty** in and around accommodation to discourage mosquitos from laying eggs

Use **insecticides** and **room sprays** indoors

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QUESTIONS PATIENTS FREQUENTLY ASK

PREVALENCE OF DENGUE

1. **Have there been outbreaks of dengue in Europe?**
   For many years only a few cases were reported however, since 2010 over 20 autochthonous dengue outbreaks have been reported in mainland Europe, the largest of which was in Italy in 2020.[7,9]
2. **Isn't dengue only present in rural regions?**
   The risk of dengue is now present in more than 125 countries worldwide, in both rural and urban regions.[5]
3. **When are mosquitoes most active?**
   Aedes aegypti mosquitoes are active during the day, particularly in the morning & evening, whilst Aedes albopictus are more active throughout the day.[23,26]

PREVENTION OF DENGUE

1. **What steps can I take while I'm away to help protect myself?**
   Wear loose, protective clothing and apply insect repellent to all areas of exposed skin. Discourage mosquitos by keeping any water containers in and around your accommodation clean and empty to decrease egg laying. Indoors, use air conditioning, insecticides or room sprays, attach screens to windows and doors, and hang bed nets to keep mosquitoes away.[22,24,25]
2. **What steps can I take before I travel to protect myself?**
   According to the WHO, vaccination should be considered as part of an integrated dengue prevention and control strategy.[23]

RISK OF DENGUE

1. **Once I have recovered from dengue, am I immune?**
   Once a person has been infected with one strain, their body will build up an immunity to only that serotype of the dengue virus.[27] *However, there are three other serotypes that you can be infected with, and immunity against the other three is only partial and temporary, meaning a person can be infected again with a different serotype. Subsequent infection by another serotype can increase the risk of developing severe dengue.*[5]
2. **Am I safe abroad if I stay in the area of my hotel/ accommodation?**
   In endemic countries, dengue mosquito vectors can be active indoors as well as outdoors, so travellers could still be susceptible to infection even if they stay inside.[1]
3. **Who could be at a higher risk of developing severe dengue than the general population?**
   Those who have comorbidities, such as diabetes, renal disease and obesity, those who have previously been infected with dengue, and the elderly could be at a higher risk of developing severe dengue than the general population.[6,16]
4. **Is there a cure for dengue?**
   There is no cure for dengue, medication and supportive care can only help manage the symptoms.[5]
5. **Can I get dengue even if I am only staying for a short time?**
   Even short stays in dengue-endemic areas have been associated with a risk of becoming infected.[14,28]

SEVERITY OF DENGUE

1. **Is it true that dengue only causes mild illness?**
   Most (around 75%) dengue infections are mild or asymptomatic, however occasionally a severe form of the disease can develop which may require hospitalisation and can be life-threatening.[5,7,19]
2. **What are some of the symptoms of dengue?**
   Travellers presenting with a high fever and any two of the following symptoms could have a dengue infection:[5]
   Severe headache, pain behind the eyes, swollen glands, vomiting, rash, nausea, muscle and joint pains.
3. **What are some of the symptoms of severe dengue?**
   Warning signs of severe dengue include:[5] *Severe abdominal pain, persistent vomiting, rapid breathing, bleeding gums or nose, fatigue, restlessness, liver enlargement and blood in vomit or stool.*
4. **Why can I contract dengue again?**
   The dengue virus has four different serotypes. After infection with one serotype, immunity against the other three is only partial and temporary, meaning a person can be infected again with a different serotype. Subsequent infection by another serotype increases the risk of developing severe dengue.[5]
5. **Could I die from a dengue infection?**
   Although dengue is a frequent cause of travel illness, severe dengue and deaths are rare.[14] *Approximately 25% of dengue-infected people develop symptomatic infections.*[7] *Within this group, ~5% may develop severe dengue*[19]*, which can take two forms: dengue hemorrhagic fever or dengue shock syndrome. People who develop dengue hemorrhagic fever have a 5% chance of death, but this can be as high as 40% if dengue shock syndrome develops.*[9]

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PRESCRIBING INFORMATION - GREAT BRITAIN

Qdenga▼ (Dengue tetravalent vaccine - live, attenuated) powder and solvent for solution for injection in pre-filled syringe. PRESCRIBING INFORMATION FOR GREAT BRITAIN (ENGLAND, SCOTLAND, WALES)
Refer to Summary of Product Characteristics (SmPC) before prescribing

Presentation: After reconstitution, 1 dose (0.5 mL) contains: live, attenuated dengue virus serotype 1: ≥ 3.3 log10 PFU [Plaque-Forming Units]/dose; live, attenuated dengue virus serotype 2: ≥ 2.7 log10 PFU/dose; live, attenuated dengue virus serotype 3: ≥ 4.0 log10 PFU/dose; and live, attenuated dengue virus serotype 4: ≥ 4.5 log10 PFU/dose. This product is produced in Vero cells and contains genetically modified organisms (GMOs). **Indication**: Qdenga is indicated for the prevention of dengue disease in individuals from 4 years of age. **Dosage and administration**: Qdenga should be administered as a 0.5 mL dose at a two-dose (0 and 3 months) schedule. The need for a booster dose has not been established. Method of administration: After complete reconstitution of the lyophilised vaccine with the solvent, Qdenga should be administered by subcutaneous injection preferably in the upper arm in the region of deltoid. Qdenga must not be injected intravascularly, intradermally or intramuscularly. The vaccine should not be mixed in the same syringe with any vaccines or other parenteral medicinal products. **Contraindications:** Hypersensitivity to the active substances or to any of the excipients or hypersensitivity to a previous dose of Qdenga. Individuals with congenital or acquired immune deficiency, including immunosuppressive therapies such as chemotherapy or high doses of systemic corticosteroids (e.g. 20 mg/day or 2 mg/kg body weight/day of prednisone for 2 weeks or more) within 4 weeks prior to vaccination, as with other live attenuated vaccines. Individuals with symptomatic HIV infection or with asymptomatic HIV infection when accompanied by evidence of impaired immune function. Pregnant women. Breast-feeding women. **Warnings and precautions**: Traceability: Name and batch number of the administered product should be clearly recorded. Anaphylaxis: appropriate medical treatment and supervision must be readily available in the event of a rare anaphylactic reaction. Review of medical history: vaccination should be preceded by a review of the individual's medical history (especially with regard to previous vaccination and possible hypersensitivity reactions which occurred after vaccination). Concurrent illness: Vaccination with Qdenga should be postponed in subjects suffering from an acute severe febrile illness. Limitations of vaccine effectiveness: A protective immune response with Qdenga may not be elicited in all vaccinees against all serotypes of dengue virus and may decline over time. It is currently unknown whether a lack of protection could result in an increased severity of dengue. It is recommended to continue personal protection measures against mosquito bites after vaccination. There are no data on the use of Qdenga in subjects above 60 years of age and limited data in patients with chronic medical conditions. Anxiety-related reactions: Anxiety-related reactions, including vasovagal reactions (syncope), hyperventilation or stress-related reactions may occur in association with vaccination as a psychogenic response to the needle injection. Women of childbearing potential: women of childbearing potential should avoid pregnancy for at least one month following vaccination. **Interactions:** Avoid vaccination with Qdenga for at least 6 weeks, and preferably 3 months, following treatment with immunoglobulins or blood products containing immunoglobulins, such as blood or plasma. Qdenga should not be administered to subjects receiving immunosuppressive therapies within 4 weeks prior to vaccination. Use with other vaccines: Concomitant administration of Qdenga with a hepatitis A vaccine and with a yellow fever vaccine in two different schedules has been evaluated in clinical studies performed in adults. Concomitant vaccines should be administered in separate syringes at different injection sites. **Fertility, pregnancy and lactation**: Qdenga is a live attenuated vaccine, therefore Qdenga is contraindicated during pregnancy. Qdenga is contraindicated during breast-feeding. No specific studies have been performed on fertility in humans. **Effects on ability to drive and use machines**: Qdenga has minor influence on the ability to drive and use machines. **Undesirable effects**: Very common (≥1/10): Upper respiratory tract infection, decreased appetite, irritability, headache, somnolence, myalgia, injection site pain, injection site erythema, malaise, asthenia, fever. Common (≥1/100 to <1/10): Nasopharyngitis, pharyngotonsillitis, arthralgia, injection site swelling, injection site bruising, injection site pruritus, influenza like illness. Other serious undesirable effects: Angioedema. **Refer to the SmPC for details on full side effect profile and interactions.** **Basic cost**: £68.75 per dose. **Legal classification**: POM. **Marketing authorisation number(s)**: PLGB 16189/0126. **Business responsible for sale and supply**: Takeda UK Limited, 1 Kingdom Street, London, W2 6BD, United Kingdom. **PI approval code**: pi-02275. **Date of preparation**: February 2023.

Qdenga▼: this medicinal product is subject to additional monitoring. Adverse events should be reported. Reporting forms and information can be found at: www.mhra.gov.uk/yellowcard. Adverse events should also be reported to Takeda at: AE.GBR-IRL@takeda.com

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PRESCRIBING INFORMATION - NORTHERN IRELAND

Qdenga▼(Dengue tetravalent vaccine - live, attenuated) powder and solvent for solution for injection in pre-filled syringe.
PRESCRIBING INFORMATION FOR NORTHERN IRELAND
Refer to Summary of Product Characteristics (SmPC) before prescribing

Presentation: After reconstitution, 1 dose (0.5 mL) contains: live, attenuated dengue virus serotype 1: ≥ 3.3 log10 PFU [Plaque-Forming Units]/dose; live, attenuated dengue virus serotype 2: ≥ 2.7 log10 PFU/dose; live, attenuated dengue virus serotype 3: ≥ 4.0 log10 PFU/dose; and live, attenuated dengue virus serotype 4: ≥ 4.5 log10 PFU/dose. This product is produced in Vero cells and contains genetically modified organisms (GMOs). **Indication**: Qdenga is indicated for the prevention of dengue disease in individuals from 4 years of age. **Dosage and administration**: Qdenga should be administered as a 0.5 mL dose at a two-dose (0 and 3 months) schedule. The need for a booster dose has not been established. Method of administration: After complete reconstitution of the lyophilised vaccine with the solvent, Qdenga should be administered by subcutaneous injection preferably in the upper arm in the region of deltoid. 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Anaphylaxis: appropriate medical treatment and supervision must be readily available in the event of a rare anaphylactic reaction. Review of medical history: vaccination should be preceded by a review of the individual's medical history (especially with regard to previous vaccination and possible hypersensitivity reactions which occurred after vaccination). Concurrent illness: Vaccination with Qdenga should be postponed in subjects suffering from an acute severe febrile illness. Limitations of vaccine effectiveness: A protective immune response with Qdenga may not be elicited in all vaccinees against all serotypes of dengue virus and may decline over time. It is currently unknown whether a lack of protection could result in an increased severity of dengue. It is recommended to continue personal protection measures against mosquito bites after vaccination. 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Qdenga▼: this medicinal product is subject to additional monitoring. Adverse events should be reported. Reporting forms and information can be found at: www.mhra.gov.uk/yellowcard. Adverse events should also be reported to Takeda at: AE.GBR-IRL@takeda.com

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PRESCRIBING INFORMATION - REPUBLIC OF IRELAND

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Presentation: After reconstitution, 1 dose (0.5 mL) contains: live, attenuated dengue virus serotype 1: ≥ 3.3 log10 PFU [Plaque-Forming Units]/dose; live, attenuated dengue virus serotype 2: ≥ 2.7 log10 PFU/dose; live, attenuated dengue virus serotype 3: ≥ 4.0 log10 PFU/dose; and live, attenuated dengue virus serotype 4: ≥ 4.5 log10 PFU/dose. This product is produced in Vero cells and contains genetically modified organisms (GMOs). **Indication**: Qdenga is indicated for the prevention of dengue disease in individuals from 4 years of age. **Dosage and administration**: Qdenga should be administered as a 0.5 mL dose at a two-dose (0 and 3 months) schedule. The need for a booster dose has not been established. Method of administration: After complete reconstitution of the lyophilised vaccine with the solvent, Qdenga should be administered by subcutaneous injection preferably in the upper arm in the region of deltoid. 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Qdenga▼: this medicinal product is subject to additional monitoring. Adverse events should be reported to the Pharmacovigilance Unit at the Health Products Regulatory Authority. Regulatory forms and information can be found at www.hpra.ie . Adverse events should also be reported to Takeda at: AE.GBR-IRL@takeda.com

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